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CONQUEST OF ECLAMPSIA

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• *The convulsive stage of eclamptogenic toxemia has been gradually eliminated in three hospitals over a period of 20 years, despite the fact that eclampsia remains one of the three most common causes of maternal mortality in the country as a whole.*

The improvement is related to the increasing frequency with which toxemia is recognized and the systematic attention given to it. The mild nonconvulsive forms of toxemia, found and treated early, are without much danger. It is the convulsive stage of the disease that does irreversible or fatal damage. A simple program of management that has been developed must be brought to bear as soon as toxic symptoms appear and must be continued until the symptoms are brought under control or the patient is delivered.

The program includes strict prenatal care, hospitalization if ambulatory care proves insufficient, induction of labor if the toxemia progresses, and cesarean section if certain indications exist. Although more knowledge of this disease is needed, the means for preventing most of the deaths that now occur are already available.

Eclampsia has been called the disease of theories and has confused the minds of medical men more than any other obstetric complication for the past century. In spite of intensive research and voluminous writings, no universally accepted concept has been evolved or method of treatment adopted. There is a certain mystery surrounding the subject that has prevented this and led to totally irrelevant suggestions by nonclinical research workers and internists who have not seen an obstetric case since their internship. Under such circumstances, it may be advisable to review the present situation with regard to the disease, to assess gains and failures as regards its control, and possibly to point out the reason for the failures and the most promising methods presently used to reduce them.

Since such a large proportion of obstetric patients are delivered in hospitals at the present time, it would seem that a study of the records of these institutions would give the best insight into the trend of the disease and the effectiveness of present-day management as opposed to that of 20 years ago. Since the patients entering institutions vary with the type of institution, it was thought advisable for the purpose of this paper to select (1) a teaching hospital, where it is presumed that the patients would receive rather above-average prenatal and delivery care; (2) a large charity-supported institution, where patients would be under good care in general but where also the poorly supervised prenatal patient in poor condition might be dumped upon the staff for definitive care; and (3) a large general hospital service, where all patients have private doctors and about equal numbers are supervised by general practitioners and specialists. In this way it was thought that a cross section of the problem could be reviewed and results of management roughly evaluated, realizing, of course, the limitation imposed by geographical distribution and by institutional variation.

In Cook County Hospital, Chicago, in 1910, where for years the mortality stood at 25 to 30%, patients developing convulsions before or after entering the hospital were purged, hot packed, stimulated, sedated, operated on, or left to die under so-called medical treatment, and the results were equally disappointing. The situation remained about the same until about 1925, when a prenatal clinic was established and toxemia patients were brought into the hospital for study. More attention was attached to reduction of protein in the diet, as advised by Whitridge Williams, in patients with preeclamptic symptoms, together with bed rest and catharsis with magnesium sulfate orally. It was advised to deliver those women who did not improve under this management and to make use of cesarean section in extreme cases. The results were considerably better than formerly, but still the mortality ranged between 15 and 20%.

TOXINS AND TOXEMIAS

About 1916 Geraghty and Roundtree described the phenolsulfonphthalein test for kidney function. Since one of the chief lesions in eclampsia is an acute nephritis, it

Chairman's address, read before the Section on Obstetrics and Gynecology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1955.

Dr. Augusta Webster and members of the Cook County Hospital staff supplied recent statistical data from that institution.

seemed probable that, if we could detect this tendency in its earlier stages, then by proper treatment we could minimize the damage to the kidney and possibly ward off the disease (fig. 1). At that time, I applied the test at the Cook County Hospital to normal pregnant women and to all types of cases of pregnancy toxemia and

Fig. 1.—Section of kidney in eclampsia, showing swollen glomeruli and epithelial degeneration in convoluted tubules.

found it to be quite reliable as a rough measure of the degree of intoxication as well as of the functional capacity of the kidney in most cases, if carefully carried out.

After making these studies it was concluded that all women who are pregnant have more toxic end-products of protein metabolism circulating in their blood than when they are not pregnant. Under normal circumstances, their excretory mechanism, unless previously damaged or congenitally deficient, rises to the challenge and excretes the additional toxins as soon as they are formed; the balance is maintained, and the patient is classed as having had a normal pregnancy. When these toxins are produced faster than they can be neutralized and excreted by the liver and kidney of the mother, they accumulate in the blood stream and produce a primary toxic effect on the cells of the kidney and liver and a similar effect on the brain, retina, and cardiac muscle (fig. 2). This lessens the functional capacity of all of these organs and decreases their efficiency, which still further augments the amount of circulating toxin, thus creating a vicious cycle.

What is this toxin, from whence does it come, and what can we do to offset its baneful effects? These are the stumbling blocks. We can best approach the problem by comparing the clinical picture of eclampsia with that of other diseases with similar features. Of these, uremia stands out as an almost exact counterpart. Edema, headaches, retinal changes, high blood pressure, vomiting, dizziness, albuminuria, suppression of urine, convulsions, coma, and death are noted (fig. 3). It is well known that the toxins in these cases are the end-products of protein metabolism that have piled up in the blood stream because of a damaged excretory mechanism, especially that of the kidney. The liver, brain, and heart muscle are also damaged, but not to the same extent as in eclamptogenic toxemia in most cases. The reason for this is that the kidney lesion is usually primary. Where then are these toxins coming from in patients with eclampsia? These patients have normal kidneys at the start of pregnancy in most cases, and furthermore they remain functionally almost normal until about the 28th week. At this time, for no apparent reason, a new increment of toxins appears that in some cases damages kidney, liver, brain, and heart so severely that the patient may die if not relieved of the pregnancy (fig. 4). Since no one has ever seen this disease in a nonpregnant female or in a male, it is hard to ignore the claims of Bartholomy in the U. S. and Young in England, who for years have insisted that the source of the toxin must be sought in the placenta and fetus as I, too, believe. They, together with Goodall of Montreal, Canada, have demonstrated hemorrhagic areas in the placenta that are thought to be a source of toxins that, when absorbed, set in motion a series of changes in the maternal organs that results in the clinical picture called eclampsia. When these areas are small and the vascular accidents occur infrequently, they give rise to mild or no symptoms. When they are larger and occur at shorter intervals, they give rise to the fulminating type of eclampsia, which is by all odds the most dangerous because it is the least understood and the most poorly handled by most physicians.

Assuming these statements to be true, it would seem that the toxins producing the clinical picture of eclamp-

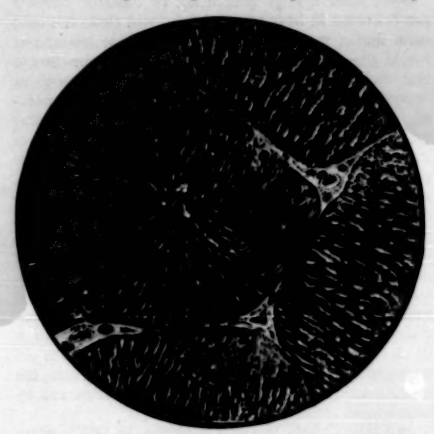

Fig. 2.—Section of liver in eclampsia (portal thrombosis and periportal necrosis).

sia, and its precursor preeclampsia, are the same or similar to those causing uremia and that in part they are derived from the activity of the maternal fetal and placental metabolism. They are retained, due to a failure of the maternal kidney to compensate for the increased load of protein end-products that must be excreted. In part

they stem from lesions in the placenta caused by vascular accidents, either thromboses or hemorrhages, of whose cause physicians are as yet ignorant. Such lesions may so pervert the function of that part of the placenta involved that it will leak toxins into maternal blood that should have been neutralized by the placenta

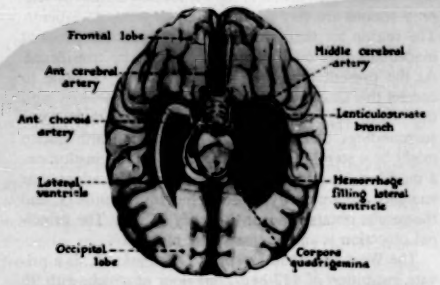

Fig. 3.—Diagrammatic sketch showing cerebral apoplexy. Rupture of lenticulostriate branch of middle cerebral artery results in hemorrhage into lateral ventricle. This cause of death in eclampsia is often overlooked.

before being excreted into the maternal blood, as well as toxic products from the degenerated placental tissue itself, which is rich in autolytic enzymes. This concept has not been previously stated as far as I know. Obviously then, if the patient with preeclamptic toxemia or eclampsia is to be managed, the procedure should be based on an intelligent concept of what has happened, what is happening, and what probably will happen in the near future if nothing is done about it.

It would seem that a logical approach would be to put the patient to bed to reduce protein breakdown from bodily activity, limit protein intake in the diet, so that there will be fewer toxic end-products of metabolism to excrete, and stimulate their excretion through the intestine by giving magnesium sulfate orally. If these measures fail or there is no clinical improvement in 48 hours, termination of the pregnancy by the most conservative method is indicated, not hesitating to do a cesarean section when special circumstances warrant it. To these measures may be added venesection when the blood pressure is high and there is no associated anemia.

RESULTS OF CONCEPT

What has been the results of this concept and this method of treatment? The Research and Educational Hospital is the teaching hospital of the College of Medicine, University of Illinois. There have been no paying patients in this institution since it opened in 1925. There has always been an outpatient clinic attended by the teaching staff of the medical school. Patients who failed to report before the 28th week of pregnancy were refused admission except in rare instances. They were delivered for the most part by interns and residents, but if any serious complication developed an attending staff member was called and remained in attendance until after the delivery. A routine management was carried out over the years so that results obtained regarding eclampsia might be comparable and thus be contrasted with results of other clinics using different methods. Briefly, it consisted of reducing protein and sodium chloride intake, restriction of physical activity, administration of magnesium sulfate by mouth, and weekly observation of blood pressure, albuminuria, edema, weight gain, and other clinical evidences of advancing or receding toxemia.

Patients were hospitalized as soon as it became evident that ambulatory care was not sufficient to control the symptoms, and bed rest was added to the above management. A phenolsulfonphthalein test was run as a rough estimate of the functional capacity of the kidney. The eyegrounds were examined, although the information so obtained was disappointing in its clinical usefulness in prognosis. Blood pressure was taken at least twice daily and in those patients with evidence of serious toxemia several times in 24 hours. Careful observation was made on the ability of the patient to read fine print and to remember current events, as well as the degree of headache, epigastric pain, nausea, and vomiting. Careful

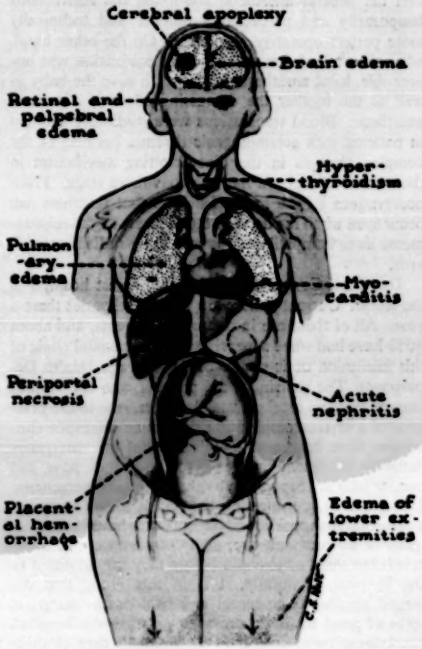

Fig. 4.—Diagrammatic sketch showing principal lesions occurring in eclamptogenic toxemia.

blood cell counts and hemoglobin level estimations were made and repeated when necessary. When, in spite of this active management, carefully carried out, marked improvement did not manifest itself within 24 to 48 hours, it was assumed that toxemia was so severe that the chance of reversing the downward trend was remote,

and therefore delivery was indicated by the most conservative methods applicable to the conditions found on physical examination at that time. Thus, if at or near term and if the uterus were found to be irritable with a soft partially effaced cervix, quinine and castor oil medical induction was tried, and, if unsuccessful, rupture of the membranes and insertion of a 4-cm. metreurynter was used for induction. Rarely, this failed to bring about active and sustained labor, in which case cesarean section was resorted to. This operation was also elected primarily in those patients in whom the cervix was found not to be "ripe," because of prematurity, or in those patients with rapidly advancing symptoms of toxemia in whom it was felt that a delay of even a few hours would significantly increase the danger of convulsive seizures, or in whom one or more seizures had already occurred.

Cesarean section was carried out with local or general anesthesia, the latter being preferred in patients having had one or more convulsion. The reason for this was that the general anesthetic controlled the convulsions temporarily and permitted a quicker and technically more perfect operative procedure. On the other hand, when the outlook for an immediate convulsion was improbable, local anesthesia was used to save the baby as well as the mother the depressing effect of a general anesthetic. Blood transfusions were studiously avoided in patients with eclamptogenic toxemia because of the complex changes in the blood-clotting mechanism in those cases that go on into the convulsive stage. From observations I have made, I believe that reactions can occur even when the donated blood meets all the requirements as to compatibility, as judged by ordinary standards.

The Cook County Hospital is the largest hospital in the world. Currently there are 12,000 deliveries there a year. All of these are in nonpaying patients, and about 60% have had some supervision in the prenatal clinic of this institution or in clinics of the Chicago Health Department. The remainder are patients who for various reasons have no local private physician, who in the presence of a severe complication such as an eclamptic convulsion have been sent to this hospital for emergency definitive treatment by their doctors, if they have had one, or who are brought in by the police as emergencies. Under these circumstances, the staff is forced to accept a rather large proportion of patients who have had inadequate or no prenatal care, many of whom are in an irreversible stage of toxemia before they are admitted to the hospital. Naturally, it is in this group that the largest number of maternal and fetal deaths occur, in spite of good medical care after entering the hospital. Until these basic defects in the prenatal care of these cases can be corrected there is no hope of completely conquering eclampsia in this institution. The basic concept must be accepted by doctors, nurses, social workers, relatives, and others in contact with a patient with toxemia, that each of them are partly responsible for her welfare if they assume the responsibility of her prenatal care and delivery. The patient herself must receive from her doctor adequate instruction on ways and means of preventing the appearance of the clinical manifestations of the disease itself in its incipient stages and also the importance of aggressive management at this time.

It must be understood that about 80% of Cook County Hospital's 12,000 deliveries last year were in indigent Negroes. Also, it is significant that cardiovascular renal lesions are very prevalent in this group of patients. The reason for this is not clear. The possible effect of inadequate diet on this problem has to be considered. At the present time little if anything can be done to correct this situation. Registration of these persons with the health department and supervision of their home surroundings and diet habits by public health nurses might be a step in the right direction. In this institution, a modified Stroganoff management has been adopted as standard treatment by most of the staff members, and the results obtained seem to justify its use. The principal objection is an increased fetal mortality.

The West Suburban Hospital, Oak Park, Ill., is a private institution of 427 beds, one floor of which, with 90 beds, constitutes the obstetric service. There are on the attending staff 12 diplomates of the American Board of Obstetrics and Gynecology, who deliver about one-half of the 3,600 private patients who are cared for in a year. The other half are delivered by general practitioners. Consultation is freely sought and given. The patients are all white and for the most part of the average middle class or higher income group. From 1934 to 1944 the obstetric staff consisted of three men who had had some formal training in obstetrics but were not actively teaching in a medical school. The great majority of the cases were handled by general practitioners. None of these men would be considered eligible for the American Board of Obstetrics and Gynecology by the present standards.

Hospital staff organization began about 1945, since which time all toxemias of pregnancy and all maternal deaths have been recorded and discussed. Almost immediately, improvement in incidence of toxemia deaths occurred and the number of cases of toxemia increased. This could only be interpreted by assuming that more attention was being focused on toxemias that occurred and that they, as a result, received more timely and better treatment. Shortly thereafter several members of the staff took and passed the American Board of Obstetrics and Gynecology examinations. Also several members of the staff became part-time volunteer teachers at Northwestern University and at the University of Illinois College of Medicine. It naturally followed that the method of management became very much like that carried out at the Research and Educational Hospital. Soon thereafter death from eclampsia almost disappeared from this institution. On the other hand, the number of patients with preeclampsia toxemia was still as high as ever. The difference in mortality, therefore, is seen in the decrease in the number of convulsive eclamptic attacks that have to be treated as well as to a better understanding of the earliest symptoms of the disease and the prompt and efficient counteractive measures previously described. Elimination of the convulsive stage by careful prenatal care and by termination of

the pregnancy conservatively if possible, and by cesarean section when the symptoms become serious in the face of what should be adequate management, has almost eliminated death from this disease in this hospital.

COMMENT

An examination of the results of treatment in each of these hospitals over the 20-year period from 1934 to 1954 shows that at Research and Educational Hospital in the first 10 years there were approximately 10,000 deliveries; among these, 1,242 patients had toxemias of various types (1,045 preeclamptic, 121 nephritic, and 75 eclamptic). Among these were three deaths due to eclampsia. In the years 1944 to 1954 there were approximately the same number of cases and one eclamptic death. In the Cook County Hospital from 1934 to 1943 there was a decrease in the death rate from convulsive eclampsia from six in 1934 to one in 1942. In 43,880 deliveries there were 32 eclamptic deaths. In the years from 1944 through 1951 there were 52,100 deliveries and 17 deaths from eclampsia. If the only patients reported were those who had been seen in the Cook County Prenatal Clinic, there would be a rate of less than one death a year from convulsive eclampsia. At the West Suburban Hospital, in the years between 1934 and 1944, there were 14,889 deliveries; 128 patients were classified as having preeclampsia and nephritic toxemias, and 39 were given a diagnosis of eclampsia, of which 5 died. From the years 1944 to 1954 there were 33,663 deliveries and 828 patients with preeclampsia and 45 with eclampsia, with one death (in a patient who also had diabetes mellitus).

It is seen, therefore, that in all of these institutions death from eclampsia has been practically eliminated through the application of knowledge already available regarding the disease. Nevertheless, in Illinois and in the United States it is still one of the three most common causes of maternal mortality. Those seeking similar reduction in maternal mortality from this cause should follow the example set in handling this problem by bringing to bear this simple management of these cases as soon as the toxic symptoms appear and continuing same until they have been brought under control or the patient is delivered.

CONCLUSIONS

In three institutions over a period of 20 years the application of present knowledge to the problem of eclamptogenic toxemia practically eliminated the convulsive stage of the disease. These patients are almost the only ones who die or who are seriously damaged by the disease. These patients are suffering from a circulating toxin originating principally in the uterus as a result of an alteration in the normal exchange of substances between the fetus and placenta and the maternal blood stream. Abnormal conditions due to vascular accidents in the placenta are the best present explanation for the appearance of an excess of the toxins in the maternal blood. In patients with mild nonconvulsive cases, found and treated early, the process is without much danger and recovery from the damage under appropriate management can be confidently predicted. In patients with severe cases, characterized by a fulminating onset, or in patients in whom the symptoms do not yield in a reasonably short time of intensive medical management, the pregnancy should be terminated before the toxemia becomes irreversible.

While the salvation of the baby is important, it should be remembered that its safety in a given case is jeopardized by continued intrauterine existence, as well as by the effect of prematurity on its extrauterine survival, and that at about the 28th week it has relatively little chance of survival in either case. It is therefore illogical to jeopardize seriously the mother's chances for survival by delaying the delivery of the fetus. At or near term, conditions are different in a great majority of cases. The fetus has an excellent chance of survival if delivered promptly and should be rescued by induction of labor or cesarean section under local anesthesia, depending on the obstetric factors surrounding the particular case.

It is desirable through research to collect more knowledge about this disease, but it is not necessary to do this to prevent most of the deaths that occur at the present time. The need at this time is a diffusion of present knowledge to the medical profession, particularly to the general practitioners, who are responsible for the care of about 85% of all deliveries in the United States. With acceptance and practice of these suggestions, I am certain it will be possible to practically eliminate one of the three most common causes of maternal mortality.

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Pheochromocytoma.—The most important item in the diagnosis of pheochromocytoma is a high index of clinical suspicion. Once the possibility is entertained, no single test can be considered reliably diagnostic or exclusive, whether positive or negative. Suspicious tests require repetition and then confirmation by different drugs. As a provocative agent, histamine appears the most reliable. Results should be checked with tetraethylammonium and methacholine, for which additional reported experiences are needed. For routine screening of hypertensive patients in large numbers, phentolamine intramuscularly or intravenously is the drug of choice. Piperoxan, because of distressing pressor responses in some patients, is most useful as a secondary check upon phentolamine responses. Dibenamine too often lowers the blood pressure of hypertensive patients to possess diagnostic significance. Patients whose blood pressures fluctuate widely should be submitted to both provocative and adrenolytic drugs at appropriate levels of blood pressure. Spontaneous fluctuations in blood pressure necessitate caution in the selection and interpretation of single tests. Alarming symptoms are sometimes produced by provocative procedures and by piperoxan; one death has followed the use of tetraethylammonium. Tests must be intelligently selected for each patient and carefully performed according to accepted techniques in the absence of drug interference. Under these conditions, pharmacologic tests will prove of greater diagnostic value and the incidence of "false" tests will be reduced to a minimum. All patients below the age of 60 years who have sustained hypertension deserve routine screening for pheochromocytoma by the use of an adrenolytic drug. Tests for catecholamines in blood and urine appear to be the most reliable of all diagnostic methods for pheochromocytoma but present the greatest technical difficulties. Pharmacologic tests, because of their simplicity, should be performed first, and each suspicious case should be checked by chemical methods, if possible, before submitting the patient to surgical exploration.—Edward S. Orgain, M.D., Pheochromocytoma: The Value of Certain Tests Used Routinely in Diagnosis, *Annals of Internal Medicine*, December, 1955.

ROLE OF THE ORTHOPEDIC SURGEON IN TREATMENT OF CEREBRAL PALSY

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• Integration of the services of specialists in the professions of medicine, education, and sociology has resulted in greatly improved care for the patient suffering from cerebral palsy. Within the medical team there must also be a balance among the specialties represented. Proper use must be made of exercise and training, of restraint and support by braces, and of surgical operations.

Analysis of several hundred operations on such patients showed that well-planned surgery contributed to the correction of deformities and to the improvement of muscle function and skill. One qualified person should be responsible for the integration of the efforts of the members of the team, in which both the physiatrist and the orthopedic surgeon are qualified to make important contributions.

It is now universally recognized that the patient suffering from cerebral palsy requires comprehensive care. This care necessitates the integration of the services of many specialists in the professions of medicine, education, and sociology. No one group or specialist may be considered the most important to this care. All are essential members of a team whose combined efforts have elevated the care of cerebral palsy to a level higher than any previously obtained.

During recent years much progress has been made toward the provision of adequate medical, educational, vocational, and institutional care for the victims of cerebral palsy. To this progress scientific research and experience have contributed greatly. Much has also been contributed by the stimulation, the continued interest, and the financial support provided by numerous organizations, such as those consisting of scientists, parents of the afflicted, and laymen devoted to this cause, and by various agencies of the government.

Medical care is frequently required by the patient with cerebral palsy because of the physical disability and deformity caused by the brain lesions of this disorder. Such physical impairments are the result of a deranged function of muscle. The measures presently known to be useful in the treatment of physical disorders are (1) passive and active exercise and the training of muscle to function; (2) the restraint and support of muscle action by the use of braces; and (3) surgical operations upon muscle, nerve, bone, and joint. The management of the disability and deformity by the use of these three measures has long occupied a prominent place in the education and the training of the orthopedic surgeon. The orthopedic surgeon is, therefore, preeminently qualified to play an important role in the care of the patient afflicted by cerebral palsy. This he may do in part through his own skills and in part by the direction of auxiliary technicians whom he has helped to train in the skills of physical and occupational therapy and the construction of braces.

A review of the prevailing tendencies in the management of cerebral palsy reveals that far greater emphasis has been placed upon treatment by physical therapy than ever before. The treatment of cerebral palsy by operation has been greatly curtailed and in some instances completely eliminated. The role of the orthopedic surgeon in the treatment of cerebral palsy has been diminished. A reappraisal of the place of the orthopedic surgeon in the treatment of cerebral palsy and an examination of the circumstances that have led to the depreciation of surgical treatment is the purpose of the following discussion.

From the Shriners Hospital for Crippled Children, San Francisco Unit, and the Division of Orthopaedic Surgery, University of California School of Medicine.

Read before the Section on Orthopedic Surgery at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

1. Little, W. J.: On the Nature and Treatment of Deformities of the Human Frame: Being a Course of Lectures Delivered at the Royal Orthopaedic Hospital in 1843: With Numerous Notes and Additions to the Present Time, London, Longman (and others), 1853.

EVOLUTION OF TREATMENT

Orthopedic surgeons have been intimately concerned with the evolution of the treatment of cerebral palsy. The first interest of the medical profession in cerebral palsy followed the classic description of this disorder in 1843 by William John Little.[1] Previous to this time the practice of bracing deformed limbs was well known and was undoubtedly used in the correction of deformities caused by cerebral palsy. By 1843 the recently developed art of physical therapy, consisting of massage, stretching, and active exercise of muscle and the reeducation of muscles to function, was coming in to general use and was applied to the patient suffering from cerebral palsy.

The first surgical measure taken against cerebral palsy was Delpech's tenotomy, as popularized by Stromeyer and Little, which was used in the correction of deformities of the feet. The use of tenotomy was soon extended to correct deformities of other joints, and from this time on the treatment of cerebral palsy by transplantation of tendons, resection of nerves, and arthrodesis of joints followed as rapidly as was permitted by the advancement of orthopedic surgery. Gradually, through research and experience, the three methods of treatment—bracing, physical therapy, and surgery—have been improved, with consequent advances in the management of the physical disabilities of cerebral palsy.

From the beginning, the discriminating orthopedic surgeon has used all three methods of treatment. He has reserved surgical treatment for use on only certain pa-

tients, such as those in whom the contractures can be promptly and effectively released, those to whom other measures have consistently failed to bring permanent correction of the deformity, and those for whom surgery is a preliminary step in the preparation for subsequent treatment by other measures. Experience has since made it apparent that surgical treatment should be reserved for the patient with pure spastic paralysis, although there are rare and exceptional circumstances in which surgical measures may be useful in the treatment of the patient with athetoid paralysis. However, the considerations that determine the use of surgery when it is a possibility have not changed with the years; in fact they have become clearer as knowledge of cerebral palsy has unfolded and experience with treatment has accumulated.

PRESENT STATUS OF SURGERY

The place of surgical treatment in the program for care of the cerebral palsied has become more clearly delineated. Surgical treatment should be delayed until the effects of bracing and training have been observed and may be withheld as long as the patient is making good progress with other therapy. This delay also permits appraisal of the patient's level of intelligence and his potential physical skills. This is not to say that surgical treatment should be denied to those of lower intelligence, but rather that the degree of improvement to be expected may be more accurately determined if the patient's intelligence is known.

Important as delay may be, surgery, when necessary, should not be delayed too long. Early operation may materially shorten or eliminate the need for physical therapy. Also, an early operation may make subsequent treatment by bracing and physical therapy much more effective than it would be otherwise. It must be recognized that the benefits of early operation may not always last through the period of growth, thus making others necessary; however, even in such situations years of physical treatment may be avoided by a series of operations. Operation may become necessary as the result of arrested progress, the onset of further deformities, or the occurrence of other complications in the course of treatment by conservative means.

In the treatment of cerebral palsy, surgery is usually but one incident in the total plan for the care of the patient. Decision regarding both the employment and the time of surgery should rest with the group of medical attendants responsible for the care of the particular patient. Much of the success of an operation depends upon the care of the patient after it has been performed, for there are few definitive operations used in the treatment of cerebral palsy. Provision should be made for adequate supervision and treatment of the patient for as long a period as may be required.

There are many operations that have by long use proved to be satisfactory in the treatment of cerebral palsy. The orthopedic surgeon is already familiar with these, but he should make certain that his co-workers are also familiar with the beneficial results that can be expected of these operations. It is only by a gradual process of reeducation that the orthopedic surgeon can convince his colleagues of the values of well-chosen operations in the treatment of cerebral palsy.

CLINICAL RESULTS

In our clinic, where a comprehensive program for the treatment of cerebral palsy is followed, a total of 354 operations has been performed on 165 patients during the 10-year period 1944-1954. The types of operation are listed in the table. These patients have been observed postoperatively by us for a period of time sufficient to make a valid evaluation in all but six instances (eight operations). In these patients the evaluation was estimated from the patients' records.

For the purpose of the evaluation of the results of this series of operations the following simple criteria were used: (*a*) the correction of deformity, and (*b*) a substantial improvement in muscle function and skill. The results were tabulated as good in 239 operations, or in 67%; fair, 65 operations, or 18%; and poor, 50 operations, or 14%. The poor results were due to technical failures, errors in surgical judgment, improper timing of the operation, overcorrection of deformity, and the causation of secondary deformity. Nevertheless, the cumulative effect of treatment by operation was considered worthwhile to the patients. By these operations the muscle function and skill of most patients were improved, bracing and crutch support were frequently made unnecessary, and the course of physical therapy was shortened. These results correspond to those found in the countless reports that are available in medical lit-

Types of Operations Used in Treatment of Cerebral Palsy in 165 Patients

Operation	Total Operations	Good	Fair	Poor	Av. Age of Patient
Strayer	89	74	9	6	7
Strayer and lengthening of tendon of Achilles	8	3	3	2	6
Popliteal neurectomy	54	34	9	11	5.2
Popliteal neurectomy and lengthening of tendon of Achilles	26	16	9	1	7.1
Obturator neurectomy and adductor tenotomy	26	18	4	4	7.2
Obturator neurectomy	6	4	2	0	6.4
Durham release abductors	24	16	3	5	10.4
Sciatic neurectomy	10	8	2	0	8.4
Median neurectomy	11	4	5	2	9
Thenar neurectomy	8	2	2	4	9
Wrist arthrodesis with tendon transfer	9	5	3	1	10
Wrist arthrodesis without tendon transfer	8	2	4	2	11.5
Triple arthrodesis foot	8	8	0	0	11
Chandler patellapexy	19	17	2	0	10.6
Posterior knee release	9	7	2	0	10.5
Tendon transfer to hand	15	8	2	5	9
Adductor tenotomy	7	5	0	2	8
Lengthening of tendon of Achilles	6	3	2	1	8
Chambers flatfoot operation	4	2	2	0	4.4
Rotation osteotomy	4	1	0	3	8.5
Tendon transfer to foot	3	2	0	1	11
Total	354				

erature and lend support to the conviction that the orthopedic surgeon should have a positive role in the treatment of cerebral palsy.

DEPRECIATION OF SURGERY

When the accomplishments of surgical intervention are reviewed, it is difficult to explain the current depreciation of this form of treatment. Specific failures have been cited to support the claim that surgery in general is unsatisfactory. Such generalizations cannot be made fairly when the circumstances leading to the failure are not presented. Orthopedic surgeons have, however, been partly responsible for the position in which they now find themselves and their specialty. In the past, many of the poor results were the result of incomplete knowledge of the basic principles of surgical treatment. As knowledge has accumulated, it has been possible to formulate principles that have progressively improved the results; however, not every orthopedic surgeon has acquainted himself with this information. Some have been so concerned with the technical aspects of a rapidly expanding specialty that they have lost sight of its fundamental principles. This latter attitude has unfortunately invaded even some of the centers that are responsible for the training of the orthopedic surgeon. One of the most serious faults of orthopedic surgeons is that many have remained rugged isolationists despite the fact that, in the treatment of cerebral palsy, the greatest advances have been the result of the formation of therapeutic teams.

Still, the delinquencies of the orthopedic surgeon are not completely responsible for the present attitude regarding the value of treatment by surgery. Others who are employed in the care of patients suffering from cerebral palsy have also influenced this attitude. Particular reference is made to the group who favor the treatment of cerebral palsy by physical therapy alone. This group includes some physicians and other professionally trained persons but is largely composed of auxiliary technical personnel whose training and experience have been restricted to the one field in which they work. Ignorance of other methods of treatment combined with inexperience leads them to place false emphasis upon the one type of therapy with which they are familiar. Their unrestricted and often ecstatic enthusiasm for this treatment is readily spread to others. Because the auxiliary worker has a particularly intimate relationship with the patient, the parents, and other technical and lay personnel, unwarranted emphasis has been placed upon the importance of physical therapy in the treatment of cerebral palsy. Furthermore, this form of treatment has too often been delegated to the therapist alone and has thus failed to benefit from the critical supervision of a qualified physician.

The effects of physical therapy on the individual patient are appraised far too infrequently. The orthopedic surgeon and/or the physiatrist are the members of the therapeutic team most qualified for these duties. No qualified person depreciates the great importance of physical therapy in the treatment of cerebral palsy; but, like surgical treatment, it must be considered as a part of the complete program of treatment of this disease. Good results have been achieved by both types of treatment used either singly or in combination. It is essential, therefore, that those who are charged with the care of the patient with cerebral palsy maintain an attitude of tolerance and broadmindedness toward all types of therapy; otherwise the patient will not receive the best treatment.

THE THERAPEUTIC TEAM

The ideals in the treatment of cerebral palsy can best be realized by the grouping of the interested specialists into a therapeutic team. One qualified person should be responsible for the integration of the efforts of the members of the team into the master plan of treatment. This person, whoever he may be, should possess wide knowledge of cerebral palsy and should know how best to utilize the services of his consultants. Only through a thoughtfully integrated and carefully supervised program of treatment can the best care be given to the patient suffering from cerebral palsy. Without careful programing there will continue to be much needless and ineffective treatment, duplication of effort, neglect of useful treatment, and unnecessary expenditure of funds upon wasted and fruitless therapy. In that part of the program that concerns the physical treatment of the patient suffering from cerebral palsy, the orthopedic surgeon has a large and important part to play.

384 Post St. (8) (Dr. Bost).

Obesity.—Treatment must be highly individualized since it may not be wise to reduce some patients rapidly. Patients recovering from operations, a recent injury or myocardial infarction or from an infection such as hepatitis or tuberculosis may need to be very cautious in their reduction procedures. It is true that one patient may lose weight on a diet of 1800 calories a day, and another may need to reduce his diet to less than 1000 calories to produce the same weight loss. The difference is usually explained by the relative differences in the amount of energy output. Some patients also tend to have a greater tendency to retain salt and water than others. In these patients a temporary restriction of sodium intake is helpful. Also, a physically active patient can usually be given a more liberal diet than would be possible for the patient who is hospitalized or who is ill or handicapped in some way. The first measure of treatment in an obese person consists of a reduced caloric intake regardless of other influencing factors. Since fat contains the largest number of calories per gram, it is most important that the fat content of the diet be restricted. It is relatively easy for the body to turn carbohydrate into fat deposits, hence the restriction of carbohydrate is of next importance. The specific dynamic action of protein is said to produce additional energy and to aid in utilization of carbohydrates. It is therefore important that a sizable portion of the diet consist of protein. . . . In many [obese] patients, hospitalization is almost a necessity to successful treatment. The advantages of hospitalization may be listed as follows: 1. Close observation including careful supervision of the diet and any special studies that may be desired. 2. A complete break from home environment, its responsibilities and its dietary habits. 3. Proof that a loss of weight at a satisfactory rate is possible despite the patient's former belief to the contrary. 4. Instruction in diet given by a dietitian skilled in this form of training and on repeated occasions is often successful when instruction in a physician's office has failed. 5. Impressions gained by the patient concerning the nature of his disorder and its hazards and unfavorable outlook and concerning the means whereby the ground gained can be maintained are often more vivid and lasting under hospital management than under management outside the hospital. Thus, a hospital period of 7 to 14 days serves as a valuable training period. Indeed, hospitalization is often as important to the long life of the patient as it is in the treatment of appendicitis or pneumonia.—L. S. Carey, M.D., Obesity, *The Medical Clinics of North America*, November, 1955.

IMPROVING SENILE BEHAVIOR WITH RESERPINE AND RITALIN

NEW APPROACH WITH USE OF METHYL PHENYLPIPERIDYLACETATE

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• *In a series of 215 patients over 60 years of age who were hard to manage because of incontinence, resistive behavior, aggressiveness, and similar abnormalities, 131 were classified as showing predominance of overactivity; they were started on therapy with reserpine, a tranquilizing drug. The 62 classified as negativistic were started on therapy with Ritalin, a psychoanaleptic drug. The remaining 22 received both drugs.*

The improvement in general was striking. Effects were sufficiently prompt to permit control of behavior by adjusting dosages and supplementing one drug with the other. The group who received both drugs was increased to 195. After four to eight months of medication it was possible to discontinue it entirely in 67 of the 215 patients without a return of the original abnormal behavior.

Neither advanced age nor cardiac disease was found to be a contraindication. The drugs not only reduced the burden of nursing care but also opened up possibilities of psychotherapy in some patients who had been confined for more than 40 years.

The advances made in medicine during the past few decades have been nothing short of miraculous. Man is healthier, and he lives better; he also lives longer. Consequently, we have produced a new and ever-increasing problem—the sociomedical complications created by these extra years. Today several million persons are involved; the number will be astronomical in the future unless prevention and control are found. An analysis of the situation reveals that abnormal behavior manifestations are predominant in those elderly individuals requiring special care, hospitalization, or institutionalization. Medical prevention and control of these abnormalities in the elderly by those closest to them, general practitioners, should be the starting point of attack.

In an effort to establish a therapeutic regimen for this type of patient that would assist in management at home, thus decreasing the need of institutionalization and the heartaches associated with it, this project was started. Our objective was to evaluate the effectiveness of reserpine (Serpasil), a tranquilizing drug, and Ritalin (methyl phenylpiperidylacetate), a psychoanaleptic drug, in controlling, ameliorating, or eliminating the abnormal behavior manifestations seen in elderly hospitalized patients. This report covers our observations after approximately 11 months of the oral administration of the drugs to 215 patients over 60 years of age who were management problems due to one or more manifestations of abnormal behavior.

SELECTION OF PATIENTS AND PRELIMINARY EVALUATIONS

Although our original investigation of the geriatric population at Traverse City State Hospital revealed no correlation between the chronological age of the patients and the degree of senescence present, the arbitrary age of 60 was chosen as our base age. The 15 female halls and cottages, often called "back-wards," which cover the complete range from seclusion to open as well as an infirmary, were chosen for the project because they represent a cross section of the usual state hospital geriatric population as well as a cross section of those geriatric patients who present the problems in behavior management in private practice. In our hospital these wards contain about one-third of the patients over 60 years of age, so that over two-thirds of our geriatric population acted as controls. Those patients from each of the 15 wards who were over 60 years of age, were known to have some behavior abnormality, or were management problems were chosen as participants, regardless of the diagnosis or pathological complications. The project, therefore, included patients with the types of behavior—overactive, underactive, and mixed—that were the basis for our use of the tranquilizing drug reserpine and/or the psychoanaleptic drug Ritalin.

Our preliminary studies revealed no correlation between aging, disease, or behavior, and there were no changes common to the group, although the largest portion of the 215 had some degree of deteriorated senile or arteriosclerotic change, with the subsequent mental symptoms and behavioral patterns associated with these changes. The number of abnormal nonprotein nitrogen values, cephalin flocculation tests, blood sugar levels, and urinalyses was compatible with a geriatric group of this size. There were no abnormalities of the total blood picture, including the number or relative proportion of the white blood cells that could be associated with the advanced ages of the group.

From the cardiac standpoint, due to our use of a drug that has some influence on the blood pressure, it is worthwhile to note that 81 of the 215 patients had cardiac abnormalities ranging from mild arteriosclerotic changes to marked electrocardiographic changes. The blood pressures of the 215 patients varied from 90/60 to 280/180 mm. Hg. The pulse rates varied from 36 per minute in two patients with heart block to 120 in several others. Forty-two of the 215 were receiving therapy with some digitalis preparation.

The ages of the 215 patients ranged from 60 to 84 years, with the average of the group being 66 plus. The length of time each patient had been in the hospital varied from one year to more than 53 years, with the average time spent in the hospital being 18 years.

From Traverse City State Hospital.

The reserpine and methyl phenylpiperidylacetate used in this project were supplied as Serpasil and Ritalin by Ciba Pharmaceutical Products, Inc., Summit, N. J.

DOSAGE PLAN

The project was limited to oral medication. We used the standard 0.1 and 1.0 mg. reserpine tablets and the standard 0.2 mg. per teaspoonful elixir of reserpine. For the Ritalin we used the 10 and 20 mg. scored tablets. No special schedules were set up for the project; the drugs were given at the regular time used by each ward for dispensing medicine. This allowed a three-time-a-day schedule. One hundred one of the 215 patients received their medicine 30 minutes to one hour before meals, and 83 of the 215 received their medicine 30 minutes to one hour after meals. The remaining 31 of the 215 tended to resist the medicine, so their tablets were crushed and put in their food or beverage at mealtime.

Our first doses were based on an evaluation of the individual patient's behavior. This was accomplished by using an 11-category check system, which covered the following points of behavior: (1) personal appearance, (2) personal care, (3) motor activity, (4) aggressiveness, (5) eating habits, (6) toilet habits, (7) night behavior, (8) socialization, (9) supervision needed, (10) cooperation in routine, and (11) rehabilitation. Those patients showing predominance of overactivity in these categories were started on therapy with reserpine. Those showing a predominance of negative characteristics were started on therapy with Ritalin. Those showing a mixed type of behavior were started on therapy with reserpine and Ritalin at the same time. At the start, 62 of the 215 were given Ritalin alone. One hundred thirty-one of the 215 were given reserpine alone, and the remaining 22 of the 215 were given reserpine and Ritalin at the same time. From previous investigation of the two drugs we felt that a lower dosage schedule would be better for this group of patients.[1] The starting dose for those receiving Ritalin alone was 10 mg. three times a day and for those receiving reserpine alone 0.25 mg. three times a day; those receiving both were given 0.2 mg. of reserpine and 10 mg. of Ritalin three times a day.

For the first 30 days the patients were checked each day and a minimal increase or decrease of each dose (0.1 mg. of reserpine or 5 mg. of Ritalin three times a day) was made every 24 to 48 hours as individually needed. By this method clinical behavior changes were gradual and controllable. We found that approximately 10% of the underactive group required more Ritalin than the 10 mg. three times a day used at the start. However, when 20 mg. of Ritalin three times a day did not produce a clinical response within two weeks, we reevaluated the patients and usually found their underactive clinical pattern was secondary to much internal anxiety and tension. By using reserpine to relieve this phase of behavior, we were then able to adjust the Ritalin for an improved over-all clinical behavior pattern.

In the overactive group we found approximately 15% who required more reserpine to control their aggressiveness and motor activity than the 0.25 mg. three times a day used at the start. By adding 0.1 to 0.2 mg. of reserpine three times a day every 24-48 hours on an individual basis, we were able to produce clinical change. In some patients this extra reserpine produced drowsiness, stuffy nose, red eyes, increased salivation, or diarrhea. However, the addition of 5 mg. of Ritalin three times a day, then, after 24 to 48 hours, the gradual reduction of the dosage of reserpine to a maintenance level eliminated these side-reactions.[2]

After a period varying from three days to three weeks it was felt that 57 of the 62 patients receiving Ritalin alone and 116 of the 131 patients receiving reserpine alone would do better if given both drugs. Consequently, in each case the second drug was added at the rate of 0.1 mg. of reserpine three times a day to the patients receiving Ritalin and 5 mg. of Ritalin three times a day to the patients receiving reserpine as individually needed each 48 hours. As the clinical behavior pattern of each patient shifted toward normal, we found she needed less reserpine and/or Ritalin. Therefore, in an effort to establish a maintenance dose level for the patients, after they showed clinical improvement, we changed the reserpine dose 0.1 mg. three times a day and/or the Ritalin dose 5 mg. three times a day every 48 hours, based upon each patient's individual improvement toward normal and the amount of overactivity or underactivity present. We have by this method been able, after periods varying from four to eight months, to discontinue use of the drugs completely in 67 of the 215 patients without a return of the original abnormal behavior.

In order to maintain the optimal improvement in the behavior of the remaining 148 of the 215, it has been necessary to continue use of the drugs, although all of them have had use of their medicaments discontinued one or more times during the 11 months of the project. At the time of writing, 136 of the 148 are receiving 0.1 to 0.2 mg. of reserpine and 5 to 10 mg. of Ritalin three times a day, while 8 of the 148 are receiving 0.5 to 1.0 mg. of reserpine and 5 mg. of Ritalin three times a day and 4 of the 148 are receiving 0.2 mg. of reserpine and 20 mg. of Ritalin three times a day.

Whenever it was necessary to adjust the medicines, we found that the clinical observations were most satisfactory, and, although behavior charts were made and laboratory work carried on in conjunction with the project, these were not found to be necessary. We were quite pleased with these findings, inasmuch as this allows for the use of these drugs by the general practitioner when he is unable to do routine follow-up laboratory procedures. To illustrate the type of patient in the project and to give examples of our method of administering the reserpine and/or Ritalin, three cases are presented.

REPORT OF CASES

CASE 1.—This patient is a 76-year-old female who was admitted in 1910. She was a talkative, wandering, disoriented, and confused woman who resisted help but was unable to help herself. She required extra nursing care, as she was a feeding problem; she was untidy and soiled most of the time. She spent most of her time in the "specialing" room for her own protection. She was started on therapy with 0.25 mg. of reserpine three times a day. Within five days she was much quieter and more friendly. Her appetite picked up, and she went to the toilet with help. Within 15 days she was sleeping in the daytime, so 5 mg. of Ritalin three times a day was added. She became more alert and stopped sleeping within three days, but her motor activity

1. Ferguson, J. T.: Improved Behavior Patterns in the Hospitalized Mentally Ill with Serpasil and Ritalin, read before Midwest Research Conference of American Psychiatric Association, Galesburg, Ill., Sept. 17, 1955.
2. Ferguson, J. T.: Treatment of Reserpine-Induced Depression with a New Analeptic: Phenidylate, Ann. N. Y. Acad. Sc. 61: 101-107 (April) 1955.

was slow. Dosage of reserpine was then reduced to 0.2 mg. She continued to slowly awaken to reality, showed a decrease in confusion, and started participating in off-ward activities during the next month. After three months the dosage of reserpine was reduced to 0.1 mg. three times a day. Her condition was without change for two weeks, then she started becoming overactive. Dosage of reserpine was then increased to 0.2 mg. three times a day, where it has remained. She has continued to slowly improve on therapy with the 0.2 mg. of reserpine and 5 mg. of Ritalin three times a day for six months. However, her age and fragility have limited her activities to the sedentary type. She has ground parole and could go home or to a nursing home.

CASE 2.—This patient is a 67-year-old mentally retarded female who was admitted in 1929. She was noisy at times and had "jerkiness" of arms and feet at times. She never bothered others or caused trouble on the ward. She is partially blind and feels her way to the dining room and toilet. She made her own bed, but otherwise spent the remainder of the time away from others in a side-room. Our aim was to eliminate the noise and excess movements while still trying to decrease her underactivity. She was started on therapy with 0.2 mg. of reserpine and 10 mg. of Ritalin three times a day. After three days she was noisier, so dosage of reserpine was increased to 0.3 mg. three times a day and dosage of Ritalin reduced to 5 mg. three times a day. Within a week her noise had subsided, so the dosage of Ritalin was raised to 10 mg. three times a day. She gradually became more friendly and started a friendship with another patient. This second patient helped her to the dining room and to entertainment. The patient seemed to be slightly underactive after another month, so the dosage of reserpine was reduced to 0.2 mg. three times a day. After four months therapy was reduced until she was without any for better than a month. However, her old pattern started to reappear, and she lost much of her mental alertness. Therapy with 0.1 mg. of reserpine and 5 mg. of Ritalin three times a day was restarted. Within four days she was back to her optimal improvement. She has remained on therapy with this dose since then. She has ground parole, which she uses with the help of her friend. She could go home or to a nursing home, but the change, due to her poor eyesight, might be too much for her to surmount.

CASE 3.—This 65-year-old female was admitted in 1922. She never talked unless prodded and was slow in movements. She needed help for all routine procedures, was a very finicky eater, and never moved by herself except to toilet. She was started on therapy with 10 mg. of Ritalin three times a day. There was no change after five days, so the dosage of Ritalin was raised to 15 mg. three times a day. There was no change at the end of four days on this regimen, so the dosage of Ritalin was raised to 20 mg. three times a day. After the third 20-mg. dose she was seen to get in line for dinner without having to be helped. She gradually started entering ward routine for the next two weeks and then started talking. However, it was felt she was showing a trend toward overactivity, so 0.1 mg. of reserpine was added to her regimen. This produced no change, so three days later the dosage of reserpine was raised to 0.2 mg. three times a day. After three days she was quieter in her activity but was talking too much. The dosage of Ritalin was reduced to 15 mg. three times a day and then after three days to 10 mg. three times a day. With this dose she has improved considerably. She participates in ward activities, enjoys television, goes to church and the movies, and went to the hospital picnic this year for the first time in 31 years. She has ground parole but will not leave the ward unless there is a group accompanied by a nurse. Her personal appearance is improved, as she likes to go to the Swap Shop (our volunteer's clothing and knick-knack shop) and pick out beads and other accessories. Her eating is normal, and she has gained weight.

RESULTS IN RELATION TO BEHAVIOR

At the start all 215 participants were chosen because they had some abnormal behavior manifestation. At the time of writing 171 of the 215 show a reduction in their original abnormal behavior while 44 of the 215 remain essentially the same. Changes within the control group during this period are negligible. As our investigation progressed we found our records were giving us an evaluation of the drugs in relation to the specific behavior covered by each category of our records. Consequently, we are reporting our observations (fig. 1 and 2) for each category in the hope that this new approach will help in establishing more specific indications for the use of reserpine and/or Ritalin in the management of the elderly patient.

Personal Appearance.—In the category personal appearance, 97 of the 215 patients were careless or were unable to take care of their manner or mode of dress. At the time of writing 81, or 83.5%, of the 97 show improvement. The most noticeable change is in the patients' ability to take an interest in what they wear and how they wear it; they also show increased interest in such things as jewelry, permanent waves, and dentures.

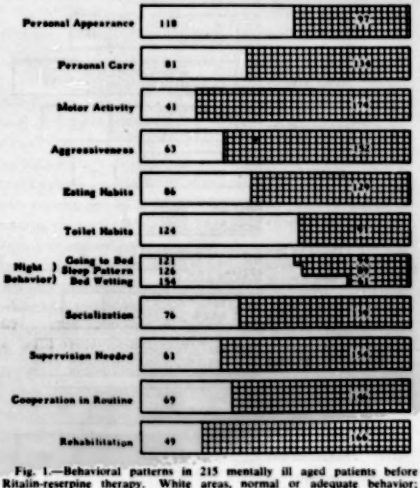

Fig. 1.—Behavioral patterns in 215 mentally ill aged patients before Ritalin-reserpine therapy. White areas, normal or adequate behavior; checked areas, abnormal behavior pattern.

Personal Care.—In the category personal care, 134 of the 215 were either resistive to or were unable to handle washing, bathing, and other personal hygiene. Now 110, or 82.1%, of the 134 show improvement. This is manifested by more personal cleanliness without help or supervision, although in most cases the total improvement is the result of retraining by the attendant-nurses of the wards.

Motor Activity.—In the category motor activity, 174 of the 215 had some abnormal overactive or underactive manifestation, such as pacing the floor, picking at themselves or others, exploring, remaining in bed, or sitting motionless unless prodded. Now 121, or 69.5%, of the 174 have improved. This is most noticeable by the decrease in movement on the wards and the decrease in patients remaining in bed or lying on the floor. There is

a marked trend toward normal motor activity in both the underactive and the overactive group.

Aggressiveness.—In the category aggressiveness, 152 of the 215 were either overaggressive to themselves or others or were underaggressive and withdrawn from others at all times. Now 109, or 71.7%, of the 152 show a marked improvement toward reality. There is less fighting and destruction and fewer accidents, along with fewer patients hiding. This appears to be the secondary result of decreased confusion and as a result has increased the patients ability to understand what is happening about them.

Eating Habits.—In the category eating habits, there were 129 of the 215 who were unable to or did not eat properly in relation to messiness, greediness, need to be fed, or proper balanced caloric intake. Now 101, or

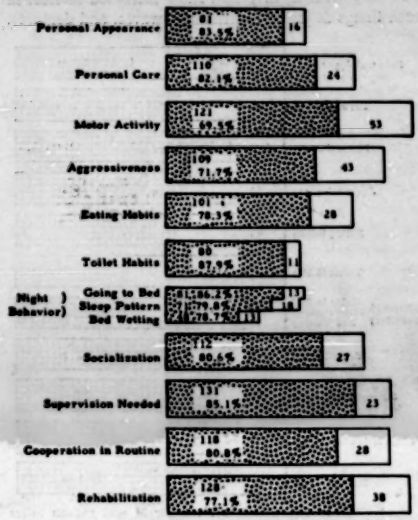

Fig. 2.—Behavioral changes after Ritalin-reserpine therapy in group showing abnormal behavior pattern (fig. 1). Dotted areas, improved with Ritalin-reserpine therapy; %, percentage of improvement with combination; white areas, unchanged.

78.3%, of the 129 show marked improvement in eating habits. There is a marked decrease in those needing to be spoon-fed and in the finicky eaters. It appears that there has been an awakening toward old manners and better balance in that which is eaten. One hundred thirty-one of the 215 have gained weight during the project. Consequently, the over-all health of the group has improved. The decrease in nursing time is quite noticeable in this category.

Toilet Habits.—In the category toilet habits, 91 of the 215 were occasionally untidy, needed toilet supervision, or had no comprehension of the toilet at all during their waking hours. Now 80, or 87.9%, of the 91 are improved. At the start there were 27 who soiled regardless of the help given them. At the time of writing 23 have stopped spontaneously, while 2 are responding to training. The decreased need for extra nursing care, as well as the decrease in laundry, has eliminated many hours of nursing time. We feel this improvement is a secondary manifestation, following an awakening to reality produced by the medicines, and is the return of normal habit patterns.

Night Behavior.—In the category night behavior, we divided behavior into three parts. There were 94 of the 215 patients who had to be helped to bed or resisted going. There were 89 of the 215 who were restless sleepers or were up wandering around during the night. There were 61 of the 215 who because of confusion or inability to help themselves wet the bed regularly or occasionally. Now 81, or 86.2%, of the 94 who had to be supervised when going to bed are improved. Some are able to completely undress and take care of themselves, while others require only to be started. There are no longer any resistive patients. Seventy-one, or 79.8%, of the 89 who were restless sleepers or were up wandering have discontinued this practice. In fact, the night nursing notes of the wards show this pattern to be rare rather than regular as it was before starting the project. Forty-eight, or 78.7%, of the 61 who wet the bed at night have stopped completely, and there is a gradual decrease in the regularity of the remaining group. Mattress replacement has been cut over 75%, and nursing time needed to help these patients has been drastically reduced. From our observations, we feel the improvement seen in this category is again the secondary manifestation of decreased confusion and the awakening of the patients toward reality and normal behavior.

Socialization.—In the category socialization, 139 of the 215 were unable to participate except in a most superficial manner or resisted any efforts at socialization. Now 112, or 80.6%, of the 139 are able to enter into more sociable relations with others, as well as to participate in supervised recreation and activities. This is best exemplified by our chapel attendance within the group: It has increased from 35 a year ago to better than 110 at the time of writing. Attendance at movies, ward parties, and off-ward entertainment has increased over 300%. This year we were able to take 167 of the group to picnics, which necessitates a 14-mile bus ride, while last year only 42 were able to go. Improvement in this category, both subjectively and objectively, has led to much more enjoyment in living for the group.

Supervision Needed.—In the category supervision needed, there were 154 of the 215 who needed supervision or help in order to complete their daily tasks. Now 131, or 85.1%, of the 154 have improved to the degree that 102 of the 131 have ground privileges and come and go on the campus as they choose. This did not happen spontaneously, as many who were able to go out refused to do so until helped and reassured by our attendant nurses. In this category, we also find less supervision needed in all facets of daily living. The members of the group make more decisions for themselves, so that in all phases of activity the nursing time and care has been reduced and we have been able to spend these

hours in constructive rehabilitation. This freedom from need of supervision has also allowed the patients to pursue their own personal pleasure outlets.

Cooperation in Routine.—In the category cooperation in routine, 146 of the 215 were either uncooperative or were unable to cooperate due to confusion or inability to understand directions. Now 118, or 80.8%, of the 146 show improvement. The improvement here parallels that in the category supervision needed, in that the rehabilitative efforts of the personnel have increased the final results as the patients awakened toward reality and lost some of their confusion.

Rehabilitation.—In the category rehabilitation, 166 of the 215 either resisted or were unable to participate in any form of rehabilitation. Now 128, or 77.1%, of the 166 show improvement in their ability to help in daily housekeeping tasks, to help in the dining room, and to go to occupational therapy. There is new interest in knitting and allied crafts to the degree that we have expanded our on-ward activities threefold. There is a new interest in music, and several of the patients now use our pianos regularly, whereas they were unable to enter into any of this activity previous to starting the project.

COMMENT

Improvement was seen at all age levels within the group so that age, per se, is no contraindication to the use of either reserpine and/or Ritalin. The length of time the patient has been ill is not a contraindication to treatment, as many of our patients in the 30 to 40 year bracket of time in the hospital have shown good improvement. None of the patients presenting abnormal physical findings at the start of the project are worse because of having participated. As a result of this, we feel that the usual physical abnormalities associated with elderly patients are no contraindication to the use of the drugs.

Throughout the period of investigation, we found no contraindication to giving the reserpine and/or the Ritalin to any of the 81 patients with cardiac disease. There was a slight gradual decrease of blood pressure in the majority of the hypertensive group receiving reserpine alone, although the hypotensive patients receiving reserpine alone showed no gross changes. The group receiving Ritalin alone and the group receiving Ritalin and reserpine combined showed no blood pressure changes of consequence. None of the patients showed any significant changes beyond normal. At the start, 72 of the 215 patients had some degree of senile tremor. At the time of writing, 61 of the 72 show improvement, manifested by a marked decrease in the rate and degree of the tremors.

During the progress of the project we conducted two withdrawal tests for verification of drug activity. In one, we substituted reserpine placebos for the reserpine in 50 patients, only to find an increase in activity within a few days. In the other, we substituted Ritalin placebos for the Ritalin in 47 patients and found most of them had reverted to their negative pattern within a matter of a few days. In each case, upon restarting therapy with the medicines we found that the patients were back to their improved level within 48 to 72 hours. No evidence of habituation was seen.

We witnessed a slight accumulative type of action with both drugs when they were used alone. This, however, was overcome by a reduction of the dose or the addition of the second drug. Consequently, we do not believe this is a true accumulation but a manifestation of change within the patient and an indication of the need for less medicine. It also leads us to believe that, when this is seen in a patient, it is an indication that the patient is establishing a balance to the degree that the drugs may be eliminated. The same is true of the so-called side-reactions reported for reserpine, inasmuch as we feel these are a manifestation of faulty balance due to improper dosage. It is rather difficult to confirm our beliefs at this time; however, with further investigation of the drugs and the physiological and biochemical actions of the brain, we feel that new light will be shed on the processes involved in mental illnesses.

There is a belief that too much therapeutic intervention in elderly patients is harmful, as it upsets the delicate balance nature has provided. This led us to be more cautious and more observant with this group; however, we believe that the chemotherapeutic management of elderly patients with reserpine and/or Ritalin should be further investigated, as many of the manifestations associated with senescence have been ameliorated or reversed during this project. We are led to believe that most of the improvement we have seen is a secondary manifestation, the primary action being a lessening of confusion and an increase in orientation, or, less specifically, a mental awakening toward reality. We were unable to pin-point this change anatomically, so we are led to believe that we are dealing with internal chemical reactions that in turn give us the manifested changes.

Our work with this group did not allow for psychotherapeutic procedures, but we feel that the complex nature of the illnesses manifested by the patients is such that one approach to the problem is not sufficient. With use of the medicines we saw a marked mental awakening of the patients to the degree that they were better able to participate; however, unless a patient was helped into new situations the improvement was minimal. This means, then, that the treatment of the elderly mentally ill patient is not chemotherapeutic alone but is a team effort in which the adjunct therapies must be used to their fullest to obtain the desired results.

CONCLUSIONS

From our work with 215 women over 60 years of age at Traverse City State Hospital, we feel that the oral administration of Ritalin (methyl phenylpiperidylacetate) and/or reserpine (Serpasil) has a definite place in the therapeutic procedures of those treating elderly patients, as these drugs have opened an entirely new and most promising approach to the problem. Further investigation of this new chemotherapeutic approach to better management of elderly patients is recommended.

PREDNISONE IN ALLERGIC DISEASES

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• *Prednisone was compared with cortisone as to potency and side-effects in 80 patients with allergic disease. Of 50 patients who had perennial chronic asthma, 41 obtained complete or nearly complete relief with the doses of prednisone that they were able to tolerate. Good or fair results were also obtained with the other types of allergic disease studied. The results were poor only in one case of seasonal allergic rhinitis.*

Most of the patients obtained improvement from prednisone in doses about one-fifth those required with cortisone. Side-effects of prednisone included gastric complaints, euphoria, increased appetite, and overstimulation. None were serious. Edema was encountered in one patient, rounding of the face in six, and urinary frequency in seven. It appeared that prednisone is far less likely than cortisone to lead to fluid retention.

Prednisone and prednisolone were first introduced in 1954 and became available for clinical use in 1955. Prednisone is the delta-1 analogue of cortisone, while prednisolone is the delta-1 analogue of hydrocortisone. Early reports on their use in rheumatoid arthritis were very encouraging. Side-effects were reported as minimal, and dosage was noted to be one-third to one-fifth that of cortisone.[1] Several reports on the use of prednisone in the treatment of allergic conditions have appeared.

Arbesman and Ehrenreich [2] reported on 17 cases of asthma, one case of perennial allergic rhinitis, and one case of chronic urticaria. In all but one, good results were obtained in the cases of asthma, while in the other cases results were poor. The average maintenance dose was 10.2 mg. of prednisone a day while the average dose for cortisone was 53.1 mg. Side-effects were minimal. Skaggs, Bernstein, and Cooke [3] report on the use of prednisone in eight cases of asthma. They concluded that the required dose was one-third to one-half that of hydrocortisone. They saw no edema, epigastric discomfort, hirsutism, facial roundness, sleepiness, or acne during the admittedly short observation period of one month. Schwartz [4] reported on the use of prednisone in two cases of asthma for approximately three months with good results and fewer side-effects when compared with other steroids.

Barach, Bickerman, and Beck [5] discussed the short-term treatment of 30 patients with bronchial asthma. They concluded that the side-effects resembled those due to cortisone and corticotropin but were of lesser extent. They used 60 to 80 mg. a day for initial doses. Robinson [6] treated four patients having atopic dermatitis with prednisone with initial doses of 60 mg. and maintenance doses of 15 to 20 mg.

Twenty-four children were treated with prednisone by Levin.[7] He concluded that prednisone was approximately twice as potent as hydrocortisone on a weight basis.

Sheldon, McLean, and Mathews [8] treated 51 patients with severe bronchial asthma with prednisone with excellent results. Thirty-six had previously received other steroids. They used a dose of 25 to 35 mg. initially. In the majority of the patients, a maintenance dose of 10 mg. a day was given. They noted improvement in 18 to 48 hours, satisfactory control of symptoms in three to four days, and maximum improvement as measured by respiratory function tests as occurring in five to seven days. Side-actions included 18 instances of moon-shaped face, 2 of insomnia, and 2 of gastrointestinal symptoms. Prednisolone was substituted for prednisone in seven patients. No difference between the two drugs was noted.

The purpose of the present investigation was to note the effectiveness of prednisone, its potency, and its side-effects compared to cortisone. This report is an analysis of the results in 80 patients with allergic disease to whom prednisone was administered. A large number of patients were observed for several months. Many of these had been on cortisone therapy previously, and in these the comparative maintenance doses of the two steroids were compared. Steroid therapy was used only in those cases where other therapy had been ineffective. Blood cell counts, urinalyses, blood pressure readings, and weight observations were made in all patients and repeated during the course of therapy. The total dose for 24 hours was divided into 6-hour portions for the first two days and 8-hour doses thereafter. No supplementary potassium was given, except where noted, and sodium restrictions were not observed in the majority of cases. In studying comparative results of cortisone and prednisone, attempts were made to change from one to the other more than once in order to obtain a more accurate comparison.

From the Allergy Clinic and Allergy Research Laboratory, Department of Medicine, Northwestern University Medical School.

The prednisone used in this study was supplied by the Schering Corporation, Bloomfield, N. J.

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6. Robinson, H. M., Jr.: Prednisone in Treatment of Selected Dermatoses: Preliminary Report, J. A. M. A. **158**: 473 (June 11) 1955.

7. Levin, S. M.: Corticotropin and Steroid Hormone Therapy of Allergic States in Children, Pediatrics **16**: 416, 1955.

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RESULTS

The therapeutic results are condensed in the following table.

Results in Eighty Allergic Patients on Prednisone Therapy

	Good	Fair	Poor	Total
Asthma, perennial, chronic	41	9	0	50
Asthma, seasonal	10	0	0	10
Allergic rhinitis, seasonal	27	4	1	32
Allergic rhinitis, perennial	1	1	0	2
Atopic dermatitis	4	2	0	6
Serum sickness (penicillin)	1	0	0	1
Chronic urticaria	1	0	0	1
Special	1	0	0	1

In the above table we have evaluated the effect on the individual manifestation. Since some patients had more than one manifestation, the number in the total results column exceeds the actual number of patients. Of the 80 patients, 6 were children under 13 years of age.

Fifty patients with chronic perennial asthma were observed. Of these 41 had good results. Our designation "good" signifies that the patient received complete or nearly complete relief with a dose of prednisone that he was able to tolerate. In actual practice, our aim was to give a maintenance dose giving results slightly less than complete. We feel that a dose that allowed the occurrence of slight symptoms now and then was preferable to one that had to be considerably greater to submerge completely symptoms at all times. "Fair" implies that, at a dose that he could tolerate well, there were still appreciable symptoms requiring medication. In some of these patients, a complication of emphysema prevented better results.

The group with seasonal asthma comprised those with pollen or mold allergy. The symptoms of these 10 patients were well controlled with prednisone therapy. The majority of the 32 seasonal allergic rhinitis patients listed were being treated primarily for their chronic or seasonal asthma. Nevertheless, this gave us the opportunity to observe the effect of prednisone in the seasonal allergic rhinitis. In 27 the results were "good," i. e., the symptoms were entirely or almost entirely controlled with reasonable doses of the drug. Four obtained "fair" results. In one the result was poor.

Of the two patients with perennial allergic rhinitis, one obtained good results and the other only fair. Four patients with atopic dermatitis had good results, and in two the relief was fair. One patient with chronic urticaria and one with a serum sickness reaction from penicillin obtained satisfactory results. The "special" case was that of a child with a low-grade fever, whose tuberculin test was positive and who had marked loss of appetite and of animation; she had previously been indefinitely diagnosed as having tuberculosis or allergy in an undetermined location. Prednisone produced subsidence of the fever, an increased appetite, and gain of weight and strength.

Irrespective of the dose, 13 patients felt either that prednisone was more effective or that it was less disturbing than cortisone. One asthmatic patient who had received 300 mg. of cortisone daily for 10 days without relief responded in two days to a dose of 30 mg. of prednisone. Three patients felt that cortisone was more effective, while in 24 there was no apparent difference.

DOSAGE

The initial dose of prednisone varied in most cases from 20 to 30 mg. per day. In a few instances it was necessary to increase that dose to 40 mg., and in one case of atopic dermatitis a dose of 60 mg. was required before improvement began. It is difficult to say what initial dose would have been effective in the majority of cases. However, the general impression is that the initial dose of prednisone needed is about 20% of that of cortisone.

The maintenance dose could be determined with much greater certainty, since the dose could be varied from time to time in the same patient. As with cortisone, we found that the dose is dependent to some extent on the type of manifestation and its severity. Nasal allergy requires on the average a higher dose than does asthma, and the generalized dermatoses require larger doses than allergic rhinitis. Severe asthma requires larger doses than mild asthma. If asthma becomes complicated by acute bronchial infection the dose of prednisone should be increased.

For their actual daily maintenance doses, 2 patients required 5 mg. of prednisone; 2 others, 7.5 mg.; 37, 10 mg.; 31, 12.5 to 15 mg.; and 8, 20 mg. It can be seen that the vast majority of our patients required a maintenance dose of 10 to 15 mg. of prednisone. When a patient got along on less than 10 mg., our experience was that in many cases he could get along without any further steroid therapy. Those requiring more than 20 mg. daily were inclined to have either poor results or a high incidence of undesirable side-effects.

In 37 patients, we were able to compare the maintenance doses of prednisone with those of cortisone. The majority of the patients had been on cortisone therapy first and, in some instances, over a long period of time. In as many instances as possible, the cortisone and prednisone were administered alternately in periods of weeks in order to get a better appraisal of the comparative effective doses. Of the total 37 patients, in one patient the ratio of the effective maintenance doses of predisone and of cortisone was found to be 1:3; in 3 others, 1:4; in 23, 1:5; in 7, 1:6; and in 5, 1:7 or less. The results indicate quite clearly that the majority of patients obtained improvement from prednisone with a dose that was 20% that required with cortisone or less.

SIDE-EFFECTS

The untoward reactions from prednisone in the main were found to be similar to those encountered with cortisone, with the exception of sodium retention and edema. In two patients with marked gain in weight and edema, the change from cortisone to prednisone produced obvious elimination of the edema and weight losses in several days. In several other patients with weight gain while on cortisone but without apparent edema, a change to prednisone produced a weight loss. This was taken as an indication that fluid retention had been present previously. However, when large doses of prednisone were used edema was produced, as in one patient with atopic dermatitis to whom a 60 mg. daily dose was administered in the beginning.

No serious side-effects were encountered in this series. Most of the side-effects occurred with the large initial doses of prednisone rather than with the lower mainte-

nance amounts. Gastric complaints of four patients consisted chiefly of burning, which was relieved by food or antacids. Euphoria, increased appetite, and feeling of increased vigor were common manifestations and not objectionable when not extreme. However, overstimulation occurred in four patients. This consisted of one or more of the following: insomnia, palpitation, dizziness, and fatigue or weakness. Excessive perspiration occurred in four patients. Urinary frequency was noted in seven. Edema was encountered in one patient, and rounding of the face in six. A side-action of interest was muscle cramps. This occurred in six patients in ages ranging from 32 to 60. In one patient this was extremely troublesome, causing waking several times during the night. The cramps were usually in the various muscle groups of the leg, although, in some, spasm of the muscles of the hand occurred when grasping objects. The mechanism of these spasms has not been ascertained, but the use of supplemental potassium therapy appeared to have little effect. We have also noted these muscle spasms in patients receiving cortisone, and three of the present series had had similar cramps from cortisone.

SUMMARY

Prednisone is a steroid with a marked anti-inflammatory action that is effective in allergic manifestations. In asthma and other allergic conditions, it is five or more times as potent as cortisone. Its side-effects from therapeutic doses are about the same as those of cortisone. In the usual doses used in allergic disease, prednisone is far less likely to lead to fluid retention.

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LONG INTESTINAL TUBES FOR OPERATIVE DECOMPRESSION AND POSTOPERATIVE ILEUS

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• *The intestinal tube here described is designed for use during surgical operations, to relieve existing distention caused by obstruction or to prevent ileus during the postoperative period. The tube bears a stylet that can be transformed at will from a flexible to a semirigid shaft. This enables the surgeon to control the tube by palpating it through the gastric wall as it advances. Passage through the pylorus, duodenum, and jejunum is thus expedited. The technique has been used more than 50 times to relieve distention in patients with intestinal obstruction.*

Operative methods of decompression are widely used at University of Minnesota Hospitals clinic for relieving distention in cases of intestinal obstruction. These were developed after unsatisfactory experiences in attempting the operative relief of obstruction in the presence of great distention of the intestine. To ease this problem in the operative management of such patients, a stylet has been developed for passage of the long intestinal tube at operation. Its use has offered a method for rapid intubation of the small intestine at surgery. This technique has obviated the necessity for an enterotomy in many patients with small intestine and right colic obstruction. Furthermore, placing the long intestinal tube into the small intestine at operation has served as an effective vent for the control of ileus during the postoperative period.

In the past, Nolan and Finley [1] have described the use of a long intestinal tube with a mercury weighted tip for intubation during operation. This tube was passed into the small intestine by the force of gravity acting on the mercury when the operating table was tilted or the abdominal viscera were gently manipulated. In our hands, this procedure has usually increased the operating time by 30 to 40 minutes or longer. Therefore, a method was developed that gives the surgeon more control over the passage rate of the intestinal tube at surgery. The purpose of this report is to describe the method and results of operative decompression with the use of a flexible stylet and plastic intestinal tubes. In addition, the special problems of management of obstructed intestine are considered.

TECHNIQUE

The apparatus and the technique of intubation are given in figures 1 and 2. The intestinal tube shown in figure 1 is 9 ft. long and made of plastic (Mayon). A stainless steel tip (*A*) is cemented and tied into its end.

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Two holes, one on each side of the plug, connect with the lumen of the tube and serve as the avenue of suction distal to the latex balloon (*B*). The balloon is inflated with air through the small plastic tubing (*C*). A hole is cut in the wall of the large tube 4 ft. from the balloon for insertion of the stylet (*D*). A steel adapter is used to occlude the opening after removal of the stylet (*E*). A short segment of intravenous tubing (*F*) serves as a connection to the suction apparatus. *G* shows the syringe in place for inflation or deflation of the balloon. The stylet is so constructed as to enable rapid advancement of the tube into the small intestine through the transformation of the flexible stylet into a semirigid shaft. The thumb lever (*H*) on the handle is attached to a flat wire that terminates at the junction of the larger (*I*) and smaller (*J*) portions of the shaft. Pressure exerted on the thumb lever transforms the proximal segment of the flexible shaft (*I*) into a semirigid column without affecting the flexibility of the distal 8 cm. of the stylet (smaller diameter shaft). This maneuver enables the operator to transform the flexible stylet into a semirigid shaft with a "flexible leading finger" and affords a safe instrument for passage into the intestine.

The flexible stylet without the controllable tip, well lubricated with petroleum jelly, is introduced through a hole in the side of the intestinal tube to within 5 cm.

of the steel tip of the tube. The tube is passed through the mouth into the esophagus with the aid of a laryngoscope. The stylet and tube are advanced until the surgeon is able to palpate the tip of the tube through the gastric wall. The surgeon's right hand is placed along the greater curvature of the stomach directing and tilting the tip of the tube toward the pylorus as the tube is advanced

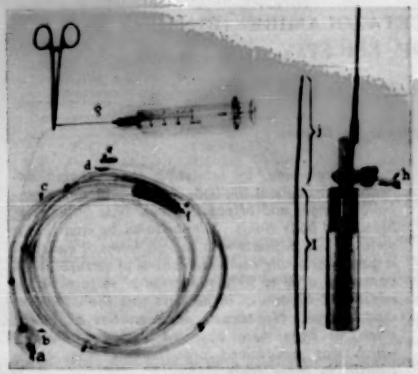

Fig. 1.—Plastic tube and flexible stylet without controllable tip, for operative intubation of the small intestine. *A*, stainless steel tip; *B*, latex balloon; *C*, small plastic tubing; *D*, hole for insertion of stylet; *E*, steel adapter; *F*, intravenous tubing; *G*, syringe in place; *H*, thumb lever; *I*, larger portion of stylet shaft; and *J*, smaller portion of stylet shaft.

(fig. 2*A*). The left hand of the surgeon directs the tube through the pylorus as the intubationist applies pressure on the thumb lever, which stiffens the stylet while the tube is advanced (fig. 2*B*). Passage into the jejunum is effected by advancing the stiffened stylet and tube from above, while the surgeon's right hand supports the greater curvature of the stomach to prevent the tube from coiling within the stomach (fig. 2*C*). The balloon is inflated with 10 cc. of air, and the tube is held stationary in the jejunum during the extraction of the stylet; however, frequently the surgeon asks to have the stylet left in position during intubation of the upper half of the jejunum, because migration of the catheter down the intestine appears to be facilitated thereby (fig. 2*D*). The small hole in the side of the tubing is occluded with a metal insert (fig. 1).

The catheter is then threaded into the intestine by holding the proximal intestine stationary and advancing the balloon-tipped catheter as it is held between the index and third fingers. During the descent of the tube, a source for continuous suction is necessary to permit evacuation of the intestinal content. If rapid decompression is desirable, the tube may be attached to a motor-driven suction through a Y-adapter. The Y-adapter provides the opportunity for frequent interruption of the high negative pressure facilitating evacuation of the intestinal content. This simple procedure can be carried out with a minimum of trauma to the intestine, and, of course, excessive traction on the mesentery of the intestine is avoided during all manipulation.

RESULTS

A recent review of all mechanical obstructions at this hospital [2] showed that this method had been used in 36 patients prior to Sept. 1, 1953. The only failure had occurred in an infant with a previously unrecognized duodenal diaphragm. Since that time, when feasible, this procedure has been employed for operative decompression of the intestine. There has been a total of over 50 patients in whom decompression has now been successfully accomplished by this method. With the stylet for rapid advancement of the long tube, decompression of the small intestine has required an average time of less than 15 minutes. There have been no complications attending this type of operative decompression.

COMMENT

The merits of intestinal decompression at surgery and during the postoperative period are widely recognized. This method of using the long intestinal tube for the relief of intestinal distention offers the surgeon a simple and rapid method of operative decompression. Furthermore, when resection of the intestine is necessary in the absence of preoperative preparation of the intestine, the tube offers an avenue for the injection of neomycin to reduce the bacterial content of the intestine. For these reasons and because postoperative ileus is not uncommon, the placement of a long tube proximal to all small intestine and ileocolic anastomoses might be justified.

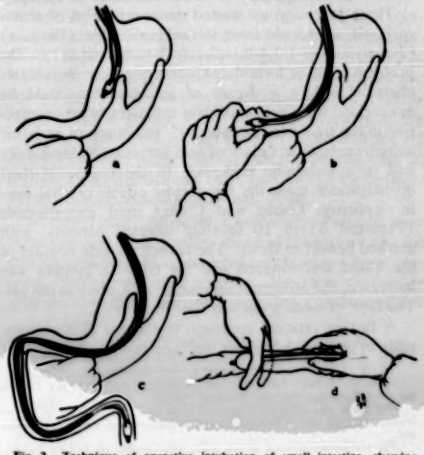

Fig. 2.—Technique of operative intubation of small intestine, showing tube *A*, advanced toward pylorus; *B*, directed through pylorus, with stiffened stylet; *C*, passed into jejunum, with stomach supported to prevent coiling of tube; and *D*, held stationary in jejunum, with balloon inflated with 10 cc. of air.

When a long tube is used during the postoperative period, gastric suction should be employed simultaneously to control distention proximal to the tip of the catheter. With the return of peristalsis, the gastric tube is removed first and the long intestinal tube is clamped for 12 hours.

2. Smith, G. A.; Perry, J. F., Jr., and Yonehiro, E. G.: Mechanical Intestinal Obstructions: Study of 1,252 Cases, Surg. Gynec. & Obst. **100**: 651, 1955.

At the end of this time the long tube can be safely removed if orally given fluids are well tolerated by the patient. Together, these precautions against postoperative ileus will improve the chance for success by placing the intestine at rest and assuring a normal intestinal circulation during healing.

SUMMARY

A rapid method of intestinal intubation at surgery has been successfully employed over 50 times for decompression of patients with intestinal obstruction. The simplicity of this procedure recommends it for general use in the passage of long tubes during surgery.

FURTHER EVALUATION OF ACETAZOLAMIDE (DIAMOX) IN TREATMENT OF EPILEPSY

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• Acetazolamide, by inhibiting the carbonic anhydrase throughout the body, causes profound metabolic changes and affects the acid-base balance of blood and body fluids. Administered by mouth in a series of 126 patients with various forms of epilepsy, it gave practically complete control of seizures in 34 cases and a 90 to 99% reduction of seizures in an additional 12 cases. In no case was the condition made worse. No serious abnormalities of blood, urine, or bone were observed during treatment, which was maintained over periods from three months to three years.

The beneficial effects were not clearly correlated with either the dosage of the drug or the level of carbonic anhydrase activity in the blood. These facts suggest that the drug may act rather directly on the metabolism of cerebral neurones.

The induction of acidosis through the use of starvation or of ketogenic and other diets was an early means of treating epilepsy. The effectiveness of other measures (ingestion of acids and acid-forming salts, inhalation of carbon dioxide, and increased muscular and mental activity) has also been demonstrated. Moreover, in epilepsy, shift of the acid-base balance of the body toward the acid side has been most helpful for young individuals and for those with petit mal seizures and the alternate spike-wave complexes of the electroencephalogram.[1] For reasons to be discussed, the methods mentioned now have a limited application in the treatment of epilepsy.

Three years ago we started an investigation of a new carbonic anhydrase inhibitor acetazolamide (Diamox) (2-acetylamino-1,3,4-thiadiazole-5-sulfonamide [2]). The problem could be formulated in this question: Would this chemical induce a degree of acidosis that could be maintained for a period of time sufficient to prove effective in the treatment of epilepsy? Inhibition of carbonic anhydrase leads to failure of acid excretion by the kidney and to a metabolic acidosis.[3] In the course of their investigations upon the therapeutic effects of vital dyes in epilepsy, Cohen and Cobb [4] used azosulfamide (Prontosil S) in 10 severely affected patients, with marked benefit to three. The carbon dioxide content of the blood was lowered and the chloride content was increased, but no significant change took place in the pH. The limit of medication was four months.

A further rational approach to the use of acetazolamide in epilepsy is the fact that a certain type of epilepsy is readily influenced by temporary variations in the carbon dioxide tension of the blood.[1] The effect of even small changes in carbon dioxide tension in such patients appears out of proportion to related acid-base shifts, and acidosis of so-called inorganic origin has not proved to be as effective as organic acidosis. Thus, we felt it worthwhile to investigate the effect of a potent carbonic anhydrase inhibitor, since inhibition of the enzyme within the nerve cells, rather than systemic acidosis, might explain the action on seizures.

We have previously reported the changes in acid-base balance of body fluids and of urine in an epileptic child given acetazolamide over a two weeks' period and the favorable effect of this drug when given to a small group of patients.[5] We have now treated 150 patients. The present report summarizes our clinical experience with 126 of these. The time interval for the other 24 is too short for appraisal (less than three months).

MATERIAL AND METHOD

The 126 patients in this series have been studied neurologically and electrographically in the seizure division of the Children's Medical Center. Eighty-two are below 12 years of age, 24 are between 12 and 19 years of age, and 20 are 20 years of age or older. The majority had been subjected, under our direction, to the accepted forms of treatment prior to being placed on therapy with acetazolamide. The previously given medicaments had proved ineffective; hence, parents and patients

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This study was aided by a research grant from the Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Md.

The acetazolamide used in this study was supplied by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

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were sophisticated about medication and the use of placebos was not considered necessary. The drug was withdrawn whenever there was doubt about its effect and also occasionally when supply was inadequate. Acetazolamide was used alone in those patients who had derived no benefit from previous therapy and was added, at least initially, to previous medication that had been partially helpful. Diet was not restricted.

TABLE 1.—*Degree of Seizure Control with Reference to Duration of Treatment*

Group	Reduction in Frequency of Seizures, %	Treatment, Mo. 0-5	5-6	6-12	12-18	18-36	Total Cases No.	%
A	90-100	..	6	9	7	12	34	27
B	80- 90	..	3	2	6	1	12	10
C	50- 80	..	9	6	4	3	22	17
D	Less than 50	7	26	11	4	..	58	46

As for dosage, tablets containing 100 mg. or 250 mg. of the drug were given by mouth. The amount ranged from 8 mg. to 30 mg. per kilogram of body weight per day. The total dose in the experimental period was from 250 mg. to 1,500 mg. given in two or three divided amounts with meals. If the amount did not exceed 500 mg., some patients took this as a single dose in the morning. At times a single large dose seemed more efficacious, but at present conclusions are not justified. The initial small amount was increased monthly until there was seizure control, unpleasant side-effects, or no effect after a trial period of two to eight weeks with a dose of 20 mg. to 30 mg. per kilogram per day. In a control series the degree of inhibition of carbonic anhydrase activity was determined for various dosage levels. Ten milligrams of acetazolamide per kilogram per day might cause as much as a 70% reduction in the activity of carbonic anhydrase in the blood as measured by a modification of the method of Philpot and Philpot as described by Ashby and others.[6] Doubling or tripling the dose increased the inhibitory effect only slightly.[5] So long as the drug was given, the carbonic anhydrase remained inhibited at an approximately constant level and returned to previous values about four to six days after the drug was withdrawn.

All patients were seen or heard from at least monthly, and they or their parents were required to complete a form giving details on seizures and symptoms before receiving more of the drug. They reported any symptoms that suggested drug intoxication by telephone. A routine examination of the peripheral blood was made monthly, and the urine was examined at the end of four weeks and later, if indicated. Patients who received acetazolamide for more than six months had roentgen ray examination for evidence of demineralization. Electroencephalograms were made before treatment was started and again after from 3 to 12 months. The period of treatment has varied from three months to three years. Those treated for the shorter time were credited with improvement only if minor seizures occurred daily in the pretreatment period. For patients experiencing less frequent attacks, the period of freedom that was judged to be significant varied with the individual. Frequent withdrawal of the drug provided further testing.

RESULTS

In the evaluation of new therapies, correction is required for a tendency to overoptimism. A large series of patients and a prolonged period of observation are essential safeguards. We have divided therapeutic results in this series of 126 patients into four groups. In group A are included patients in whom control was practically complete; in group B, those in whom reduction in frequency of seizures was 90% or more; and in group C, those whose seizures benefited by at least 50% control; while in group D are included all patients in whom percentage reduction in frequency of attacks was less than 50%. Display of the number and the percentage distribution of patients and the periods of treatment for each group are contained in table 1. Thirty-seven per cent had received at least 90% benefit and only 46% less than 50% benefit or none. No one's condition was made worse. The proportion of persons more than 90% improved increased progressively with length of treatment, presumably because medication was not continued in the face of failure to control.

Clear correlations between clinical response and either the dosage of acetazolamide or the level of carbonic anhydrase activity in the blood was not observed. Neither did an increase of the dose above 500 or 750 mg. increase its effectiveness. Failure could not be attributed to poor intestinal absorption because the degree of inhibition of the enzyme was similar in favorable and unfavorable cases. Much variability of results was encountered. A person with results categorized A or B for at least three months of therapy might subsequently escape control and require change of therapy to other medicament. Such a person might respond favorably if the drug was reinstated. A person well controlled for six months or more might remain free of seizures after all medicine was withdrawn. In at least half of the patients benefited acetazolamide was used alone.

Seizure Types, Alone or Combined.—Patients were separated into three groups: those with a history of petit mal seizures only; those with petit with other seizure patterns, such as myoclonic jerks or convulsions; and those with seizures other than petit mal. No pronounced difference in response to acetazolamide was observed in these three groups of patients, except that somewhat more favorable results were obtained in patients who experienced mixed types of seizures, usually a combination of grand and petit mal; 46% of these persons were classed in groups A and B as against 27% of those with

TABLE 2.—*Degree of Seizure Control with Reference to Seizure Type, Single or Combined*

Seizure Control, Degree	Petit Mal Seizures Alone (29 Cases) No.	%	Petit Mal and Other Types (41 Cases) No.	%	Other Than Petit Mal (56 Cases) No.	%
A	7	24	12	29	15	27
B	1	3	7	17	5	9
C	4	14	8	20	9	16
D	17	59	14	34	27	48

6. Ashby, W.; Garzoli, R. F., and Schuster, E. M.: Relative Distribution Patterns of 3 Brain Enzymes, Carbonic Anhydrase, Choline Esterase and Acetyl Phosphatase, Am. J. Physiol. 170: 116, 1952.

petit mal seizures alone and 36% of those with convulsive or psychomotor seizures. In judging results, both of the latter types were considered (table 2).

Individual Seizure Types.—Additional correlation was attempted between therapeutic effect and four individual seizure types as they existed or coexisted in patients at the onset of treatment; namely, petit mal 70; myoclonic, akinetic, and massive myoclonic, 42; convulsive (including focal) attacks, 73; and psychomotor (including a few autonomic attacks), 25. The total of 210 indicates that some persons had more than one type of seizure. The percentages for the combined A and B groups (90 to 100% controlled) for the four different groups of seizures are as follows: petit mal, 38%; other forms of the petit mal triad, 48%; convulsive, 37%; and psychomotor, 40%. The relatively good effect for the second group is in spite of a relatively large factor of brain damage. Of the 12 children with massive myoclonic jerks, 8 (60%) received control classed as A or B (table 3).

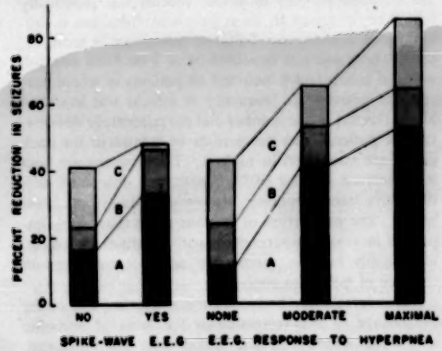

Fig. 1.—Degree of seizure control with respect to fast spike-wave representation in the electroencephalogram (*left*) and with respect to the degree of activation of the electroencephalogram by means of hyperventilation (*right*). The ordinate indicates the percentage reduction in the number of seizures under acetazolamide medication. The letters A, B, and C indicate groups of patients with 99 to 100%, 90 to 99%, and 50 to 90% control respectively.

TABLE 3.—*Degree of Seizure Control with Reference to Single Seizure Type*

Seizure Control, Degree	Petit Mal Seizures Alone (70 Cases)		Akinetic and Myoclonic (42 Cases)		Convulsive (73 Cases)		Psychomotor (25 Cases)	
	No.	%	No.	%	No.	%	No.	%
A	19	27	12	29	21	29	7	28
B	8	11	8	19	6	8	3	12
C	12	17	7	17	13	18	5	20
D	31	45	15	35	33	45	10	40

Electroencephalographic Patterns.—In order to disclose the relationship, if any, between therapeutic response and electrographic patterns, patients were separated into groups (table 4). Recordings of 12 were incomplete because, usually due to youth, hyperventilation was not performed. Patients with some pattern other than a 3 per second spike and wave pattern in the electroencephalogram numbered 44 (second column). These included slow spike-wave, paroxysmal slow, focal slow, or focal fast patterns. Those with a fast spike-wave pattern numbered 70. Clinical improvement classed as A or B was obtained in 46% of patients with 3 per second spike-wave formations compared with 25% of the group without this pattern in the electroencephalogram (left-hand portion of figure 1). Analysis was made of the fast spike-wave group. Persons whose electroencephalogram responded to hyperventilation with pronounced "activation" of the record (increased number of spike-wave discharges or of high voltage slow waves) obtained most relief from medication. Improvement classed as A or B (90 to 100% seizure control) occurred in only 24% of persons with no electroencephalographic activation, in 53% of those with moderate activation, and in 64% of those with extreme response; that is, many more spike-wave discharges and immediate continued "buildup" of waves (right-hand portion of figure 1).

TABLE 4.—*Degree of Seizure Control with Reference to Fast Spike-Wave Representation in Electroencephalogram and Response to Hyperventilation*

Seizure Control, Degree	No 3-per-Second Spike-Wave		Did Not Perform Hyperventilation		Activation by Hyperventilation, Degree					
					None		Moderate		Maximal	
	No.	%	No.	%	No.	%	No.	%	No.	%
A	7	16	4	33	3	11	7	41	13	52
B	4	9	0	..	4	13	2	12	3	12
C	7	16	2	17	5	19	2	12	5	20
D	26	59	6	50	16	57	6	35	4	16

These results seem to show that the patient who stands the best chance of being helped by acetazolamide is the one whose electroencephalogram not only exhibits a spike-wave dysrhythmia but also displays prompt slowing of waves and a profusion of spike-wave discharges in response to the alkalosis caused by overventilation. The preferred position of patients with petit mal seizures has been generally recognized. The advantage of an activation of the electroencephalogram by means of induced alkalosis has been suggested but not previously demonstrated.

Several patients whose electroencephalograms were taken serially have shown electroencephalographic as well as clinical improvement. Figure 2 shows sections from successive electroencephalograms of a 12-year old boy. All were made during hyperventilation. The left-hand section was made before the administration of acetazolamide. Abnormally slow waves and 3 per sec-

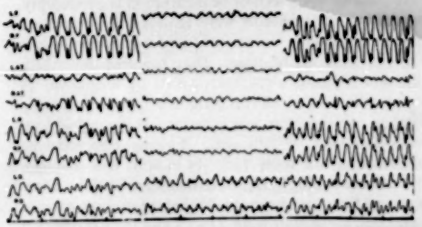

Fig. 2.—Samples of the electroencephalogram of patient taken before, during, and after treatment with acetazolamide. Letters refer to the monopolar placement of electrodes. In the original recording a deflection of 5 mm. equaled 50 mv.

ond waves with stubby spikes are nearly continuous. The midsection was made 11 days after starting therapy with acetazolamide at a dose of 500 mg. per day. The right-hand section was made 12 days later, therapy with acetazolamide having been stopped; the pretreatment abnormality and the boy's seizures have returned.

Influence of Brain Damage.—Patients who exhibited clear evidence of some organic cause were grouped together. Pathological lesions included those from progressive degenerative disease and injuries sustained in a paranatal period. Some patients had gross neurological signs, others only mental retardation, and still others only consistently lateralized electroencephalographic abnormalities. These patients with evidence of organic cause and the 75 without evidence of brain damage differed but little in therapeutic response to acetazolamide. Favorable results were only slightly better in the undamaged group, a finding not in accord with experience with standard antiepileptic agents.[7]

Influence of Genetic History.—Patients with a family history of epilepsy or allied disorders numbered 50; those without numbered 76. Results classified A and B (more than 90% improvement) characterized 52% of the group with positive family history and 28% of those without such history. Fast spike-wave discharges were present in 70% of the electroencephalograms of those with a family history and in 62% of those without. This difference would hardly explain the better response of the group with a family history of epilepsy. Comparison was then made of the patients with electroencephalographic records that displayed maximum response to hyperventilation, again the difference found being hardly significant. Of the 18 patients in the group with a positive family history, A or B results occurred in 72%. Of the 24 patients with a negative history, this improvement occurred in 50%.

Side-Effects.—Evaluation of the effectiveness of a new drug is difficult, and associated toxic reactions make treatment hazardous. Conclusions must be tentative, and there is no substitute for expenditure of time and accumulation of experience in an increasing number of patients. The youthfulness of patients and the many years of medication that may be required demand caution in assessing potential toxicity. Nevertheless, during our three years' experience with acetazolamide we have encountered few toxic effects. This is the testimony also of persons who have used acetazolamide for other ailments over long periods of time.[8] Our investigations were confined to the blood, urine, and skeleton, and these do not necessarily rule out the possibility of chronic intoxication. Although symptoms of potassium or other electrolyte depletion have not been detected in our series, further study, particularly of growing patients, is necessary to rule out this eventuality when acetazolamide is administered continuously.

Our record of side-effects encountered is only an approximation, since much of the information was contained in progress reports rendered by patients. Whenever feasible, a causal connection with the drug was tested objectively by its withdrawal and reinstatement. Of the 14 side-effects noted, some patients reported several. Three effects (reported by 59 persons) were favorable: "behavior improved," "more alert," and "sleep improved." Unfavorable effects in order of frequency were: drowsiness, 19; anorexia, 17; irritability, 11; and from 5 to 2, rash, tingling, dizziness, poor behavior, enuresis, vomiting, ataxia, and hyperpnea.

COMMENT

Beginning with periods of starvation 30-odd years ago, acidifying and dehydrating measures produced in various ways have stood the test of time in demonstrating a beneficial influence on epileptic seizures. Acid ash and ketogenic diets, ingestion of acids and acid-forming salts, inhalation of carbon dioxide, restriction of fluids—these measures, assisted or not by the addition of the cation-exchange resins, have each shown a degree of success. Each of these measures has certain drawbacks. The diets are unpleasant and difficult to maintain. The action of the acidifying salts is often short-lived and probably depends mostly on the dehydrating effect. Use of the resins is complicated by excessive interference with cation absorption, and revision of dosage calls for periodic electrolyte determinations of the blood. In contrast, acetazolamide is simple to administer; it has a wide margin of safety, produces a smaller systemic acidosis, and the effect is surprisingly well-sustained.

The present experience concerns 126 patients whose seizures had in many cases proved refractory to standard therapy and who took acetazolamide for periods up to three years. For a significant number, the drug provided control of seizures and of electrical seizure discharges. Fortunately, trial of the drug on seizures of patients preceded the test of its effectiveness against pentylenetetrazol (Metrazol)-induced seizures in mice. Everett and others [9] found the mouse test especially valuable for evaluation of "anti-spike-wave" drugs, but in our tests acetazolamide has afforded very little protection against pentylenetetrazol-induced seizures of mice.[10]

Our clinical studies do not afford clues as to mechanisms involved in the therapeutic effect of acetazolamide. Does the antiepileptic action depend only upon a sustained mild systemic acidosis and concomitant dehydration, or is there a more localized and direct action upon the carbonic anhydrase of the brain? Certain doubts oppose the simple assumption that only acidosis and dehydration are the responsible agents. For one thing, the initial diuretic effect of the drug, when given in the dosage named in this study, is not usually long maintained.[11] Again, preliminary clinical observations in epileptic [12] or cardiac patients [8a] have failed to show therapeutic effects comparable to those from a similar degree of acidosis induced by means of ammonium chloride.

7. Lennox, W. G., and Davis, J. P.: Clinical Correlates of the Fast and Slow Spike-Wave Electroencephalogram, Pediatrics 5: 626, 1950.

8. (a) Friedberg, C. K.; Taymor, R.; Minor, J. B., and Halpern, M.: The Use of Diamox, a Carbonic Anhydrase Inhibitor, as an Oral Diuretic in Patients with Congestive Heart Failure, New England J. Med. 248: 883, 1953. (b) Nadell, J.: Effects of Carbonic Anhydrase Inhibitor "6063" on Electrolytes and Acid-Base Balance in 2 Normal Subjects and 2 Patients with Respiratory Acidosis, J. Clin. Invest. 32: 622, 1953. (c) Leaf, A.; Schwartz, W. B., and Relman, A. S.: Oral Administration of a Potent Carbonic Anhydrase Inhibitor ("Diamox"): Changes in Electrolyte and Acid-Base Balance, New England J. Med. 250: 759, 1954.

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10. Lombroso, C. T., and Millichap, J. G.: To be published.

11. Footnote 3c and 8c.

12. Lombroso, C. T., and Davidson, D. T., Jr.: Unpublished data.

In animals, extreme metabolic acidosis elevated the threshold to electroshock seizures by only 14%,[13] and no change in threshold was obtained from a mild metabolic acidosis. Similarly, intravenous injection of acid or of alkaline solutions produced no appreciable modification of the pentylenetetrazol-induced convulsive discharges.[14] Of course, shifts in acid-base balance may differ both in their origin and in their effect upon body physiology. For instance, changes in pH brought about by variations in carbon dioxide tension may alter the speed of nerve conduction and nerve sensitivity to stimulation, but such effects are absent or minimal if the same change of pH is obtained without altering carbon dioxide tension.[15] The mode of distribution of carbonic anhydrase in various structures of the central nervous system * presumably has a physiological basis, and the inhibition of this enzyme at the cellular level in the brain may have a more significant effect upon neuronal physiology than the genera' systemic pharmacological effects of the drug.

SUMMARY AND CONCLUSIONS

Acetazolamide (Diamox), an inhibitor of carbonic anhydrase, has been given to 126 epileptic patients. Treatment extended for periods of from three months to three years. In 37% seizures were reduced by at least 90%, in 17% they were reduced 50 to 90%, and in 46% they were reduced by 50% or less. None were made worse, nor was any serious side-effect or abnormality of blood, urine, or bone encountered. The degree of improvement was not related significantly either to a personal history of brain damage, a family history of epilepsy, or the type of seizure. Benefit was greatest for patients having 3 per second spike-wave discharges of the electroencephalogram. Maximum benefit occurred if the alkalosis induced by hyperventilation of the lungs resulted in maximal increase of spike-wave discharges and of "buildup" in the record. In some patients, well controlled for at least three months with therapy, seizures later returned. Reinstitution of therapy with the drug later often reproduced the initial favorable response. The beneficial effect on seizures may be a result of the acidosis or the dehydration induced or of inhibition of enzyme action in the neurones. Acetazolamide should prove useful not only as an adjuvant in the therapy of epilepsy but also as a means for further investigation of the role of acidosis and of carbonic anhydrase in the metabolism of normal and abnormal brain tissue.

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13. Hendley, C. D.; Davenport, H. W., and Toman, J. E. P.: Effect of Acid-Base Changes on Experimental Convulsive Seizures, Am. J. Physiol. 153: 580, 1948.
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AURICULOTEMPORAL SYNDROME

GUSTATORY SWEATING DUE TO MISDIRECTION OF REGENERATED NERVE FIBERS

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and
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• Two patients exhibited profuse sweating limited to the temporal region on one side. The sweating accompanied salivation during the mastication of food and necessitated wiping the area repeatedly at every meal. In both patients there was a history of parotitis following abdominal surgery. Tests with acetylcholine, pilocarpine, and histamine in one patient led to the conclusion that, in the process of recovery from parotitis, regenerating parasympathetic salivary fibers must have been misdirected into the sweat glands, which normally have a sympathetic innervation, and that these responded thereafter in a manner to be expected from their abnormal, dual nerve supply. Both patients were relieved permanently of this annoying syndrome by intracranial division of the glossopharyngeal nerve.

The auriculotemporal syndrome is provoked by a salivary stimulus and consists of flushing and sweating of the area of skin supplied by the auriculotemporal nerve. It occurs as a late sequel of injury of this nerve. Because of the bizarre nature of the disorder and its interesting physiological implications, the mechanism of this form of gustatory sweating has aroused considerable debate in medical literature. It has been variously ascribed to aberrant regeneration of divided salivary fibers into degenerated sweat fibers, to supersensitivity of denervated sweat glands, to transaxonal excitation of damaged sweat fibers by damaged salivary fibers, and to increased irritability of damaged sweat fibers. The syndrome develops after an illness or operation that has damaged the auriculotemporal nerve, such as parotid abscess, excision of a parotid tumor, or resection of the descending ramus of the mandible. The onset of the syndrome usually is after an interval of time long enough to allow for regeneration of the damaged nerve; in only a single reported case did the symptoms begin earlier. Study of the two cases reported here indicates that the auriculotemporal syndrome is due to reinnervation of sweat glands by parasympathetic salivary fibers.

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Drs. Francis Boyer and J. Portugal Pinto, former fellows in neurological surgery, contributed to this study.

ANATOMY

The auriculotemporal nerve arises from the mandibular branch of the trigeminus immediately below the foramen ovale. It then runs laterally and posteriorly to the medial side of the neck of the mandible, where, closely in contact with the capsule of the parotid gland, it turns upward between the mandibular condyle and the external ear. It supplies sensation to the skin of the temple and also carries sympathetic and parasympathetic fibers. Some twigs of the auriculotemporal nerve communicate with filaments of the facial and of the greater auricular nerve. Its parasympathetic component originates in the inferior salivatory nucleus and travels by way of the glossopharyngeal nerve to Jacobson's nerve, to the tympanic plexus, to the small superficial petrosal nerve, to the otic ganglion. Postganglionic fibers from the otic ganglion pass to the nearby auriculotemporal branch of the mandibular nerve and travel in it to the parotid gland to supply secretory and vasodilator innervation.

The sympathetic component reaches the auriculotemporal nerve as a postganglionic branch from the superior cervical sympathetic ganglion and carries vasoconstrictor fibers to the parotid gland and vasoconstrictor and sweat fibers to an area of skin corresponding to the sensory distribution of the auriculotemporal nerve. Thus, this sensory nerve is unique in that in the portion of its course adjacent to the parotid gland it contains postganglionic parasympathetic and postganglionic sympathetic fibers.

PHYSIOLOGICAL CONSIDERATIONS

When an end-organ is paralyzed by interruption of its postganglionic axon, there are four known mechanisms by which it may be reactivated: (1) by the development of supersensitivity to a circulating chemical mediator; (2) by regeneration of the postganglionic axon; (3) by reinnervation by an axon that originally supplied another end-organ, and (4) by transaxonal excitation of a regenerated axon by the action potential of an axon supplying another end-organ. Actually, it seems probable that the resumption of activity of the end-organ, at least during some phase of the recovery period, is due to a combination of all four mechanisms. In addition, it must be borne in mind that a state of increased irritability (lowered threshold of excitability) exists at the point where a nerve is compressed by a scar or other process. List and Peet [1] believe that this is the explanation of the auriculotemporal syndrome. They state that scars in the parotid gland, and perhaps attempts at regeneration in the strangulated twigs of the auriculotemporal nerve, "maintain a local condition of abnormal irritability of cholinergic fibers." However, it is obvious that this increased irritability cannot operate alone, although it may enhance any of the four mechanisms described above.

In searching for an explanation of the auriculotemporal syndrome, it is essential that we confine ourselves to these four known mechanisms by which an end-organ can be reactivated following interruption of its postganglionic axon. Since simple reinnervation by the original axon could not be responsible for this bizarre phenomenon, this mechanism can be dismissed without further comment. The theory that the syndrome is the result of anatomic misdirection of salivary fibers into sweat fibers is supported by Ford and Woodhall,[2] Hogeman,[3] Boyer and Gardner,[4] and other earlier authors. The denervation-sensitization theory is favored by Freedberg, Shaw, and McManus,[5] by Haxton,[6] and by Langenskiöld.[7] The theory that the auriculotemporal syndrome is due to transaxonal excitation of sympathetic sweat fibers by parasympathetic salivary impulses is supported by Chorobski.[8]

In 1949 Boyer and Gardner [4] described two cases of gustatory lacrimation, or "crocodile tears," a condition allied to gustatory sweating. In these cases the syndrome developed after surgical resection of the large and small superficial petrosal nerves on the floor of the middle fossa. The large superficial petrosal nerve carries preganglionic secretory fibers of seventh nerve origin to the lacrimal gland. The lesser superficial petrosal nerve carries preganglionic secretory fibers of ninth nerve origin to the parotid gland. Relief of gustatory lacrimation was afforded by dividing the ninth nerve intracranially. These authors assumed that the relief in these two cases by resection of the ninth nerve proved that the syndrome was due to the arrival in the lacrimal gland of impulses from aberrantly regenerated ninth nerve fibers that had originally innervated the parotid gland. However, as was later pointed out by Chorobski,[8] the phenomenon could just as well have been due to cross stimulation of normally regenerated fibers as to anatomic cross regeneration of the involved nerve fibers.

The following significant facts regarding the auriculotemporal syndrome have been established: 1. There is usually impairment of sensation in the distribution of the auriculotemporal nerve, indicating that it has been partially or completely interrupted. 2. The sweating response to heat is usually diminished in the involved area as compared with that in the uninvolved area on the opposite side, although it may be normal or even increased. 3. The syndrome is abolished temporarily by procaine block of the auriculotemporal nerve, at the level of the tragus, as shown by several authors, and more lastingly by a resection of this nerve, as shown by Hogeman.[3] 4. It is not abolished by a procaine block of the cervical sympathetic chain. 5. Profuse sweating in the area of distribution of the involved auriculotemporal nerve is caused by administering pilocarpine parenterally, and the syndrome is eliminated by atropine. 6. There is marked supersensitivity of sweat glands in the distribution of the

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affected auriculotemporal nerve to the intradermal injection of acetylcholine. This was demonstrated by Langenskiöld,[7] in 1946, and by Freedberg, Shaw, and McManus,[8] in 1948, and was present in case 2, described below.

REPORT OF CASES

CASE 1.—A woman, aged 54, presented herself on Feb. 17, 1950, complaining of attacks of headache associated with blurred vision and nausea and vomiting, which were believed to be migraine. She also gave a history of gustatory sweating. She stated that she had had left parotitis following a right salpingectomy for ectopic pregnancy 21 years before. The parotitis subsided without draining, but several months later she observed flushing and profuse sweating of the skin over the left temple and cheek while eating. This was distressing and necessitated wiping her cheek with a napkin numerous times during each meal, especially if sour or spicy foods were being consumed.

Examination revealed cutaneous hypesthesia in the distribution of the left auriculotemporal nerve. Within a few seconds after she began to eat, the skin of the involved area became erythematous and perspiration formed on it. The phenomenon was especially pronounced when sour or spicy foods were eaten. Because of our belief that this syndrome was due to misdirection of interrupted ninth nerve salivary fibers into the peripheral ends of degenerated sympathetic sweat fibers, we advised intracranial division of the left glossopharyngeal nerve. This was done on March 16. As soon as the patient began to eat the after the operation, it was apparent that the phenomenon of flushing and sweating over the left cheek had been abolished. She was discharged from the hospital on the 12th postoperative day. When seen one month later, she stated that flushing and sweating during eating had not reappeared. But, when she was tested with lemon juice held in the mouth, a faint reddening of the involved area appeared for 90 seconds. Thirty seconds later a few scattered minute beads of perspiration formed, but these failed to enlarge even with continuation of the strong gustatory stimulus. The response was so mild compared with the preoperative phenomenon that the patient was unaware of it. Five years after operation the patient reported that there had been no recurrence of the syndrome.

Fig. 1. (case 2).—Area of gustatory sweating outlined by Minor's starch-iodine. In addition to the area supplied by the auriculotemporal nerve (above the zygoma), there also is sweating in a contiguous area below, which is supplied by filaments of the greater auricular branch of the cervical plexus. Filaments of these two nerves are known to anastomose in the substance of the parotid gland.

The explanation as to why relief in this case was not complete probably lies in the fact, demonstrated by Reichert and Poth,[9] that, while most of the salivary fibers in the auriculotemporal nerve are of ninth nerve origin, there are also some seventh nerve salivary fibers that supply the parotid gland.

CASE 2.—A woman, aged 52, presented herself on Oct. 30, 1953, with the chief complaint of frequent vomiting for two and a half years. This symptom proved to have a psychoneurotic basis. A secondary symptom was flushing and sweating in the right temporal area during eating. A gastroenterostomy had been done in 1932 because of a stenosing peptic ulcer. This was followed by postoperative parotitis, with an abscess that pointed below the angle of the mandible. The patient was quite ill at this time, with severe swelling of the entire right side of the face. Some months later, she became aware of a feeling of warmth, followed by profuse perspiration, in the right temporal region during eating. Perspiration ran down the side of the face, and she had to mop it frequently during each meal. Since onset this had occurred with every meal, without exception. Tart flavors, especially a baked apple, brought on a vigorous response.

On examination the patient was found to be a poorly nourished, anxious woman whose face was asymmetrical, due to atrophy of the right parotid gland. With involuntary blinking, there occurred a simultaneous twitch of the right angle of the mouth, indicating cross regeneration of facial nerve fibers, interrupted probably at the time of the parotitis. There was a scar behind the angle of the right mandible, where the parotid abscess had drained. The skin was of normal texture and appearance in both auriculotemporal regions. There was no demonstrable impairment of tactile or pain appreciation. She was given a baked apple to eat, and, after the first couple of bites, there was a slight flush over the right temporal and infrazygomatic areas. In one and a half minutes beads of perspiration also appeared, and, as she continued to eat, sweating became profuse and ran down to the angle of the mandible. The involved area was in the distribution of the auriculotemporal nerve and a contiguous area below, extending to the angle of the mandible, which is supplied by filaments of the greater auricular nerve (fig. 1).

Tests.—One hundred micrograms of acetylcholine chloride was injected intradermally above the zygoma in each auriculotemporal area. On the right side the injection caused immediate flushing, extending for 1 cm. around the injection site. This was followed in 45 seconds by beading and then by profuse sweating confined to the flushed area, which continued for one and a half minutes. Intradermal injection on the left side caused flushing to the same extent, degree, and duration but was at no time associated with sweating. This test was interpreted as indicating sensitization to acetylcholine of the sweat glands in the distribution of the right auriculotemporal nerve.

After the face was coated with Minor's starch-iodine, the patient was placed in a warm room and covered with blankets. She was given 10 grains (0.6 gm.) of acetylsalicylic acid and two cups of hot tea, and hot water bottles were applied to the body. Control temperature measurements in each auriculotemporal area, made with a surface thermometer, showed no difference between the two sides throughout the test. Within five minutes of the beginning of the heating, a well-defined area of sweating appeared in the right auriculotemporal area. At this time no sweating was demonstrable on the forehead or on the left side of the face and relatively little on the covered portion of the body. This pattern of sweating persisted for 30 minutes, after which the test was discontinued. This demonstration of enhanced thermoregulatory sweating in the distribution of the right auriculotemporal nerve could be explained on the basis of supersensitization of sweat glands to impulses arriving over regenerated or residual sympathetic nerve fibers, or, perhaps, simply to hypertrophy of local sweat glands due to chronic overactivity.

After the patient's face again had been coated with Minor's starch-iodine, she was given ½ grain (30 mg.) of pilocarpine hydrochloride subcutaneously. Flushing of the face and the anterior wall of the chest appeared within three minutes. After four minutes the patient noticed a generalized feeling of warmth, most pronounced on the right side of the face. At five minutes a tiny spot of perspiration appeared on the right side of the forehead, almost simultaneously with one above the right ear. At five and a half minutes a similar blue spot was present on the left side of the forehead, and at six minutes the right auriculotemporal area turned solidly blue and small punctate spots appeared over the right cheek and right side of the chin. There were fewer and smaller punctate blue areas on the left side of the face. This pattern persisted during the hour of observation. We concluded that sweat glands of the right auriculotemporal area showed a definitely enhanced response to pilocarpine.

The patient was given 0.25 mg. of histamine phosphate intravenously. This caused a severe generalized flush, but there was

9. Reichert, F. L., and Poth, E. J.: Recent Knowledge Regarding Physiology of Glossopharyngeal Nerve in Man with Analysis of Its Sensory, Motor, Gustatory and Secretory Functions, Bull. Johns Hopkins Hosp. 53:131-139 (Sept.) 1933.

no sweating over any portion of the face. This patient did not show the sweating response to histamine that Tankel [10] observed in a case of gustatory sweating involving the entire side of the face.

Operation and Course.—The right ninth nerve was exposed intracranially and divided between silver clips on Nov. 30, 1953. After operation it was apparent that sweating on eating was abolished. On the seventh day after the operation the intradermal test with acetylcholine was repeated, using the same technique. Injection on the right was followed immediately by flushing and by profuse sweating. Sweating covered a larger area and was more profuse than at the preoperative testing and lasted six instead of one and a half minutes. Injection of the same dose on the left side caused redness but again failed to elicit sweating. The conclusion was: Resection of the right ninth nerve resulted in further sensitization of the sweat glands in the right auriculotemporal area. The patient was discharged from the hospital on the eighth postoperative day, and she reported later that on this day she noted recurrence of sweating in the right auriculotemporal area on eating.

On examination five weeks after operation, sweating was repeatedly observed when she ate various tart substances, but it was more delayed, much less pronounced, and involved a much smaller area than before the operation. On each occasion there was no visible flushing. The sweating was usually confined to an area 2 cm. in diameter just above the right zygoma, but on one occasion there was also perceptible sweating in an area that extended down to a point just above the angle of the mandible. Intradermal acetylcholine elicited the same response that it had on the seventh day after operation. Seventeen months after operation the syndrome was still present to the same degree, and it was eliminated by the administration of 1/150 grain (0.4 mg.) of atropine sulfate 30 minutes prior to a meal. The patient had not been tested with atropine prior to this.

COMMENT

We believe that the observations made in case 2 disprove the theory that the auriculotemporal syndrome depends solely upon supersensitivity to acetylcholine, for, although the involved area was supersensitive to intradermal injection of acetylcholine prior to operation, supersensitivity was more pronounced after the syndrome had been largely abolished by ninth nerve section. Furthermore, this increase in supersensitivity to intradermal injection of acetylcholine following operation implies that the sweat glands had, in fact, been denervated by ninth nerve section. Therefore, after the original illness, secretory fibers of the ninth nerve must actually have reached and innervated the sweat glands in this area. If the syndrome in this patient had been due to cross stimulation of sweat fibers by impulses carried in neighboring salivary fibers, then interruption of the salivary fibers would not have caused further denervation-sensitization of the sweat glands.

That some cases of gustatory sweating may be due to transaxonal excitation rather than to actual anatomic misdirection of fibers cannot be denied. That this is not the sole mechanism is indicated by the fact that the syndrome seldom appears until sufficient time has elapsed following the nerve injury to permit regeneration of the damaged fibers and, once established, the condition is, with very few exceptions, permanent. This is in contradistinction to that undisputed example of transaxonal excitation, causalgia, which was so beautifully demonstrated by the work of Granit, Leksell, and Skoglund [11] and by Doupe, Cullen, and Chance.[12] In causalgia early onset is the rule, and spontaneous recovery is not infrequent. Causalgia could not be explained on the basis of misdirection of regenerating nerve fibers, inasmuch as the involved fibers are sensory afferents (dendrites) and sympathetic efferents (axons). In other words, were anatomic union to occur, there would result two cell bodies, joined by a combined dendrite and axon, sending impulses in opposite directions. Most evidence indicates that a nerve fiber can conduct in only one direction and that a functional union cannot occur between an afferent and an efferent fiber.

As regards denervation-sensitization, sweat glands in the involved auriculotemporal area in case 2 did show sensitization to injected acetylcholine before ninth nerve section. In an effort to learn whether sensitization due to sympathetic denervation may also play a role in the auriculotemporal syndrome, a series of sympathectomized patients was studied. All had had cervical sympathectomies, usually bilateral, with removal of the superior cervical ganglion on one side and interruption of the cervical sympathetic chain below the ganglion on the other. As described in case 2, 100 mcg. of acetylcholine was injected intradermally in the auriculotemporal areas of each patient.

Three patients were tested on the fourth or fifth postoperative day. In two, denervation was postganglionic on one side and preganglionic on the other. Acetylcholine did not produce sweating on either side in either patient. The third patient had a postganglionic denervation on one side and no operation on the other. The denervated side, again, showed no sweating response to acetylcholine; the innervated side showed slight sweating immediately about the injection site.

Seven additional patients had been operated upon from 18 months to three years before testing. Six of these patients had a postganglionic denervation on one side and a preganglionic denervation on the other; all failed to show a sweating response to acetylcholine injected into both auriculotemporal areas. The seventh patient had a preganglionic denervation on one side and no operation on the other; acetylcholine elicited slight sweating in the innervated auriculotemporal area but not in the denervated area. One of these patients had had one ninth nerve sectioned intracranially six months before testing in addition to cervical postganglionic sympathectomy; acetylcholine failed again to elicit sweating. The sweating response to intradermal injection of acetylcholine in normally innervated auriculotemporal areas was definite but was minor compared with the striking response observed in the involved area in case 2.

None of these sympathectomized patients described sweating on the face even during hot weather, and none had noted gustatory sweating. The study of these cases therefore shows that sympathectomized sweat glands do not exhibit increased sensitivity to acetylcholine as do sympathectomized salivary glands, as described by Simeone and Maes.[13] Can this be related in some way to the fact that the normal sweat glands have only a

10. Tankel, H. I.: Case of Gustatory Sweating, J. Neurol. Neurosurg. & Psychiat. 14: 129-133 (May) 1951.

11. Granit, R.; Leksell, L., and Skoglund, C. R.: Fibre Interaction in Injured or Compressed Region of Nerve, Brain 67: 125-140 (June) 1944.

12. Doupe, J.; Cullen, C. H., and Chance, G. Q.: Post-Traumatic Pain and Causalgic Syndrome, J. Neurol. Neurosurg. & Psychiat. 7: 33-48 (Jan.-April) 1944.

13. Simeone, F. A., and Maes, J. P.: Sensitization of Submaxillary Gland by Sympathetic Denervation, Am. J. Physiol. 125: 674-679 (April) 1939.

sympathetic supply, whereas the salivary glands have both a sympathetic and a parasympathetic supply? We believe that gustatory sweating of the face following excision of the superior cervical ganglion, as was reported by List and Peet [13] and by Wilson,[14] must be due not to the sympathectomy per se, but to the development of aberrant connections between neighboring vagal secretory fibers that were traumatized by the operation and remaining sympathetic neurons.

Our observations in sympathectomized patients accord with those of Simeone, Mentha, and Rodrigues,[15] who found that the sweating response of the cat's paw to pilocarpine and to electric stimulation disappeared after chronic denervation. They concluded that this exception to Cannon's law of denervation is only apparent, that detrimental gland and vascular changes mask the denervation-sensitization that is probably present. We believe it is unlikely, however, that disuse atrophy could develop within four to five days after cervical sympathectomy, by which time some denervation-sensitization should appear. Injected acetylcholine in our cases

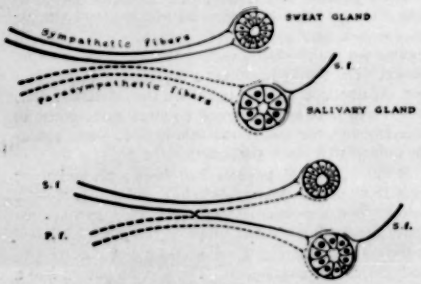

Fig. 2.—The sweat gland normally is supplied only by sympathetic fibers, whereas the salivary gland has, in addition, a parasympathetic supply (*S. F.*, sympathetic fiber; *P. F.*, parasympathetic fiber). After interruption of the auriculotemporal nerve, cross regeneration results in the development of a dual nerve supply to the sweat glands, which then begin to respond like salivary glands. That is, they discharge in response to a gustatory stimulus; they become exquisitely sensitive to acetylcholine and to pilocarpine, and after ninth nerve section the supersensitivity to acetylcholine is further enhanced.

elicited no response after this interval, though a small response was observed on the normally innervated side. This lack of sensitivity of sweat glands after sympathetic denervation contrasts sharply with the clear-cut sensitization to injected acetylcholine and to pilocarpine in the involved area in case 2. It proves that the auriculotemporal syndrome is not due to denervation-sensitization per se.

One hypothesis that might be advanced to explain the exaggerated response to parenteral administration of pilocarpine and to intradermally injected acetylcholine is that, since sweating occurs vigorously and often in an area of gustatory sweating, the response to these stimuli could be expected to become enhanced in the same manner in which overactivity results in hypertrophy or more powerful function in other organs. Against this hypothesis is the fact that further sensitization to injected acetylcholine appeared after section of the ninth nerve, a denervation phenomenon not present when the normal sympathetic nerve supply of the sweat gland was interrupted in other patients. It may be that the salivary fibers of seventh nerve origin also going to these sweat glands were sufficient in number and activity to maintain the hyperresponsive state.

In view of the existing sensitization of sweat glands in the involved auriculotemporal area in case 2, it is likely that the enhanced response to heat was dependent upon residual sympathetic fibers reaching and stimulating the sensitive glands, or upon these fibers cross stimulating parasympathetic salivary fibers innervating the sweat glands.

Sir Henry Dale [16] has recently summarized the evidence indicating that humoral neurotransmitters that are unknown at the present time must exist because those identified to date cannot account for all types of neuroeffector activity. We believe this postulate is necessary to explain some of the observations made in the present study, namely, that when sweat glands become innervated by parasympathetic salivary fibers, they then show a quantitatively different response to injected acetylcholine and to pilocarpine. This is explained if we assume that the cholinergic chemical mediator released by the parasympathetic salivary fiber is different from that released by the sympathetic sweat fiber and that laboratory acetylcholine is chemically similar to the mediator released by salivary fibers but dissimilar to that released by sweat fibers. Therefore, sweat glands, having developed a true parasympathetic nerve supply, begin to behave like salivary glands in that they become much more sensitive to pilocarpine and acetylcholine (fig. 2).

One clear fact is that reinnervation of sweat glands by parasympathetic salivary fibers somehow results in a strikingly enhanced response to various stimuli. At this time the mechanism or mechanisms involved are obscure; whether one of those suggested may be responsible is only speculative; probably several are involved.

In case 2, as in several cases reported by other authors, gustatory sweating as a sequel to injury to the auriculotemporal nerve was not strictly limited to the cutaneous distribution of this nerve but involved also an area below, which is innervated by the facial branches of the great auricular nerve, a branch of the cervical plexus. Because this involvement beyond the distribution of the auriculotemporal nerve has been observed in other cases, Langenskiöld [7] objects to the term "auriculotemporal" syndrome. The explanation of sweating in this adjoining area is clear when we recall that filaments of the great auricular nerve enter the substance of the parotid gland to anastomose with the auriculotemporal nerve.

SUMMARY

The auriculotemporal syndrome, a form of gustatory sweating, was largely relieved by intracranial division of the ninth nerve in two patients. Sweat glands in the in-

14. Wilson, W. C.: Observations Relating to the Innervation of the Sweat Glands of the Face, Clin. Sc. **2**: 273-286 (July) 1936.
15. Simeone, F. A.; Mentha, C., and Rodrigues, H. A.: Responsiveness of Sweat Glands After Denervation by Preganglionic Ramisection, Ganglionectomy and Peripheral Nerve Section, Am. J. Physiol. **165**: 356-364 (May) 1951.
16. Dale, H. H.: Junctional Transmission of Nervous Effects by Chemical Agents, Proc. Staff Meet. Mayo Clin. **30**: 5-20 (Jan. 12) 1955.

volved auriculotemporal area in the one case tested showed sensitization to intradermal acetylcholine; further sensitization developed after section of the ninth nerve. This development of denervation-sensitization is strong evidence that ninth nerve fibers had been supplying the sweat glands; the syndrome, therefore, in all probability was due to misdirection of regenerated parasympathetic salivary fibers into the sweat glands. This resulted in a dual nerve supply to the sweat glands, similar to that of normal salivary glands. Besides sensitivity to intradermally injected acetylcholine and, presumably, to the parasympathetic humoral effector, there was an enhanced response of the sweat glands to parenteral injection of pilocarpine and to systemic heating, the latter probably depending upon a combination of residual sympathetic innervation and sensitization to the humoral effector.

Sensitization of sweat glands, associated with establishment of a parasympathetic nerve supply, stands in sharp contrast with the complete failure of sweat glands to show sensitization after acute or chronic sympathetic denervation. It is hypothesized, therefore, that establishment of a true parasympathetic nerve supply to sweat glands is associated, perhaps in causal relationship, with appearance of sensitization to a variety of stimuli and that the substance released by parasympathetic salivary nerve endings differs chemically from the cholinergic substance released by cholinergic sympathetic nerve endings.

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SUCCESSFUL HOMOTRANSPLANTATION OF THE HUMAN KIDNEY BETWEEN IDENTICAL TWINS

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• *A patient whose illness had begun with edema and hypertension was found to have suffered extreme atrophy of both kidneys. Because of the steady worsening of the condition and the appearance of uremia with other unfavorable prognostic signs, transplantation of one kidney from the patient's healthy identical twin brother was undertaken.*

Preparations included collection of evidence of monozygosity and experimental transplantation of a skin graft from the twin. During the transfer of the healthy kidney it was totally ischemic for 82 minutes. Evidence of functional activity in the transplanted kidney was obtained.

The hypertension persisted until the patient's diseased kidneys were both removed. The homograft has survived for 11 months, and the marked clinical improvement in the patient has included disappearance of the signs of malignant hypertension.

This report documents the successful transplantation of a human kidney from one identical twin to another. The function of the homograft remains excellent 12 months after the operative procedure. Previous attempts at renal homotransplantation, both clinically and experimentally, have been unsuccessful with one exception. In dizygotic cattle twins, a kidney transplant has survived and functioned for at least nine months. Success in this instance, however, presumably resulted from the production of an acquired mutual tolerance to each other's tissues by the mingling of fraternal protein in the common placental circulation.[1] Transplantation of the kidney in dogs and other animals rarely maintains function for more than a 10-to-14-day period in spite of vigorous attempts to modify the presumed antibody response that results in rejection of the homograft. Similarly, permanent function has not been maintained in a human renal homograft,[2] although in one such instance adequate renal function in a transplanted kidney has persisted for five and a half months.[3] The ultimate cause for rejection in such cases is in all probability differences in individual tissue specificity. Since, however, skin homografts between identical human twins have survived permanently,[4] it might be expected that renal homotransplantation might also be successful when performed between identical twins. The following case history describes such an event.

REPORT OF A CASE

A 24-year-old, white, single male was apparently in excellent health until 14 months before his first admission to the Peter Bent Brigham Hospital. Except for scarlet fever at age 5 without apparent complications, the history was noncontributory. A few months prior to his discharge from military service, the patient noticed some puffiness about the eyes on awakening in the morning, and on a routine physical examination some elevation of blood pressure was noted. During a five-month study period while at the Boston Public Health Service Hospital, he remained essentially asymptomatic except for epistaxis. Physical examination was negative except for a consistently elevated blood pressure averaging 170/100 mm. Hg. Pertinent laboratory findings included persistent 2 to 3+ proteinuria. The urinary specific gravity was fixed at 1.010 and microscopic hematuria

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The table and figure 1 have been omitted from THE JOURNAL and will be included in the authors' reprints.

1. Billingham, R. E.; Brent, L., and Medawar, P. B.: Acquired Tolerance of Skin Homografts, Ann. New York Acad. Sc. **59**: 409, 1955.

2. Lawler, R. H., and others: Homotransplantation of the Kidney in the Human: Supplemental Report of a Case, J. A. M. A. **147**: 45 (Sept. 1) 1951. Küss, R.; Teinturier, J., and Milliez, P.: Quelques essais de greffe de rein chez l'homme, Mém. Acad. chir. **77**: 755, 1951. Michon, L., and others: Une tentative de transplantation rénale chez l'homme: aspects médicaux et biologiques, Presse méd. **61**: 1419, 1953.

3. Hume, D. M.; Merrill, J. P.; Miller, B. F., and Thorn, G. W.: Experiences with Renal Homotransplantation in the Human: Report of 9 Cases, J. Clin. Invest. **34**: 327, 1955.

4. Brown, J. B.: Homografting of Skin: With Report of Success in Identical Twins, Surgery **1**: 558, 1937.

and cylindruria with occasional red blood cell casts were found in all urine specimens. Blood urea nitrogen level ranged between 75 and 100 mg. per 100 cc. Hemoglobin level varied between 7 to 10 gm. per 100 cc. Phenolsulfonphthalein excretion was less than 1% in two hours, and an intravenous pyelogram revealed no dye excretion on either side. X-ray of the chest showed the lungs to be clear and the heart normal in size and shape. After seven transfusions of whole blood he was discharged improved. Five months later he was readmitted again to the Boston Public Health Service Hospital and appeared pale and chronically ill. The blood pressure now varied between 160/80 and 208/120 mm. Hg. The retinal vessels showed narrowing of the arterioles with changes in caliber and occasional arteriovenous compression. He was discharged after a three-day period and readmitted six weeks later because of nausea, vomiting, headache, and general muscular aches. At this time he appeared more seriously ill, and marked pallor of the skin was evident. The blood pressure was 172/90 mm. Hg; retinal vessels showed narrowing and arteriovenous compression; and lungs were clear. The heart appeared to be slightly enlarged to the left. There was a grade 2 blowing systolic murmur over the entire precordium. The remainder of the physical examination was normal. Pertinent laboratory data follow. Hemoglobin was 6.7 gm. per 100 cc. and hematocrit 20%; urine showed 3+ protein, 2+ sugar, and 5-25 red blood cells per high-power field on spun sediment. There were occasional granular and hyaline casts. The blood urea nitrogen was 185 mg. per 100 cc. His course was characterized by persistent nausea and vomiting and on the third hospital day he had a generalized convulsion. In succeeding days he became increasingly drowsy, disoriented, and irritable and had several convulsions. Since the patient had a twin brother, it was suggested by Dr. David C. Miller of the U. S. Public Health Service that the possibility of homotransplantation of a kidney should be considered. For the investigation of this possibility, he was transferred to the Peter Bent Brigham Hospital on Oct. 26, 1954.

On admission the initial blood pressure was 140/90 mm. Hg. The patient appeared thin, pale, drowsy, and extremely disoriented. The remainder of the physical examination and laboratory data were consistent with that outlined above. Urine culture grew out Escherichia coli and enterococci. The patient continued to be restless and unable to tolerate oral feedings and became overtly psychotic. On the fourth hospital day he was treated by external dialysis with the artificial kidney [5] for a four-hour period. A good chemical response was obtained and 36 hours later the patient's sensorium had cleared and he was cooperative and able to take diet and medicaments by mouth.

On the 15th hospital day, full-thickness skin grafts, 2.5 by 2.5 cm., were exchanged between the twins. A control autograft was placed proximally and the homograft was placed 1 cm. distally, allowing a bridge of normal tissue to intervene between the two grafts. On the following day the patient was discharged feeling well on a diet containing 50 gm. of protein and no added salt. He was followed at weekly intervals in the outpatient clinic, continued to show hypertension, and gradually developed the manifestations of congestive heart failure for which he was digitalized with some improvement. On Dec. 12, 1954, however, he was readmitted to the Peter Bent Brigham Hospital because of marked increase in signs and symptoms of his congestive heart failure. Physical examination at this time revealed a blood pressure of 220/146 mm. Hg. There was 3+ pitting edema of the lower legs up to the knees. Bilateral basal rales were present. The liver edge was tender and was palpated 4 cm. below the right costal margin. There was slight periorbital edema and the optic fundi now showed a 2 diopter papilledema with exudates and hemorrhages. The heart was enlarged to the left with a loud diastolic gallop heard over the entire precordium. A chest film showed marked cardiac enlargement with evidence of fluid at the base of the right side of the chest. During the next three days, 350 cc. of turbid, amber fluid was removed from the right side of the chest and the patient received three units of packed red blood cells. He was started on therapy with parenterally given protoveratrine. On this therapy there was marked clinical improvement.

5. Merrill, J. P., and others: The Use of the Artificial Kidney: I. Technique, J. Clin. Invest. 29:1 412, 1950.

On Dec. 16, 31 days after the original skin transplant, biopsy study of the homograft was done. In both gross and histological section the transplanted tissue appeared to have survived as normal skin. Because of this evidence of tissue compatibility and ancillary observations suggesting that the twins were monozygotic, on Dec. 23 a normal left kidney was removed from the healthy twin and transplanted to the patient. (Previous hospitalization had disclosed the absence of discoverable disease in the healthy twin and confirmed the presence of two normally functioning kidneys free of infection.)

The postoperative course of the donor was uneventful, and he was discharged on the 14th hospital day. The recipient tolerated the operative procedure well and, soon after the anastomoses were completed, clear urine was noted draining freely from the transplant. Nine days after surgery the intravenous injection of sodium indigotindisulfonate (indigo carmine) showed prompt appearance in good concentration in the urine from the transplanted kidney and no excretion from the patient's own kidneys. During the course of the following month, the homograft appeared to function well and began to hypertrophy. The patient was discharged from the hospital on the 37th postoperative day. He had gained 11 lb. (5 kg.) and was edema free. The blood urea nitrogen was 14 mg. per 100 cc. and the resting blood pressure, 120/60 mm. Hg. The chest was clear and the heart size normal. The serum carbon dioxide combining power was 25 mEq. per liter and the serum concentrations of sodium, chloride, potassium, calcium, and phosphate were all within normal limits. The phenolsulfonphthalein excretion was 18% in 15 minutes and 48% in two hours. Urinalysis at the time of discharge showed a trace of albumin, 4 to 6 white blood cells, and a rare blood cell per high-power field. Urine culture grew out Proteus vulgaris.

After discharge the patient's appetite was good and he had no edema, dyspnea, or orthopnea. Blood pressures ranged from 130/80 to 160/88 mm. Hg. The optic disks were normal, and the retinal vessels became normal, although a few old scars persisted in the optic fundi. Because of continued mild bacilluria and pyuria, the patient was begun on methenamine mandelate (Mandelamine) therapy. An excretory urogram performed two months after the renal homotransplantation showed prompt excretion of the injected dye in good concentration from the transplanted kidney but no detectable excretion by the two diseased kidneys.

Because of persistent mild hypertension, the patient was admitted to the Peter Bent Brigham Hospital for the third time three months after renal homotransplantation. At this time the initial blood pressure was 152/90 mm. Hg. The patient appeared healthy and completely asymptomatic. There had been further gain in weight and muscle development. The palpable mass of the homograft in the right lower quadrant had hypertrophied to half again its original size. The electrocardiogram showed disappearance of the changes of left ventricular hypertrophy. The hematocrit was 48%, blood urea nitrogen 14 mg. per 100 cc., and carbon dioxide combining power 23 mM. per liter. On the fifth hospital day a left nephrectomy was performed. The kidney weighed only 49 gm. and was covered by a markedly thickened capsule that was fibrosed and scarred. The cortex was markedly diminished in size and the microscopic section showed the majority of the glomeruli to be completely fibrosed. The renal parenchyma showed diffuse atrophy and fibrosis with disappearance of tubular elements and the appearance was that of diffuse advanced chronic glomerulonephritis. The patient was discharged 12 days after operation feeling entirely well. However, because of the persistence of mild pyuria and mild labile hypertension, he was readmitted for the fourth time on June 14, 1955, five and a half months after renal homotransplantation. On the seventh hospital day the patient underwent an uneventful right nephrectomy. The right kidney weighed only 29 gm. and showed the typical changes of advanced diffuse chronic glomerulonephritis with little functioning parenchyma remaining. On discharge the patient's appetite was good; he had gained more weight and was essentially asymptomatic. At the present time his blood pressure ranges from 125/70 to 146/82 mm. Hg. He weighs 25 lb. (11.3 kg.) more than his initial preoperative weight. He carries on unlimited activity and has no apparent physical disability. The urinary sediment is negative, although his 24-hour protein excretion is 4.5 gm.

COMMENT

The transplantation of functioning tissue from one individual to another of the same species has, with few exceptions, not been successfully accomplished to date. Successful transplantation has been occasionally reported in the case of embryonic thyroid,[6] parathyroid,[7] and in one instance adrenal [8] tissue. The successful transplantation of bone and blood vessels depends not on their survival as living tissues but on their ability to act as bridges over which recipient tissue may grow. Because of its particular structure and the fact that it is frequently transplanted into an avascular field, corneal transplants in man, however, do survive as living tissues in a large percentage of cases.[9] The immune response leading to the rejection of homografts is incompletely understood. Circulating cytotoxic antibodies cannot be measured in significant amounts. It is probable, however, that antibodies to donor tissue are formed by the recipient and that these are removed by the homograft so rapidly that they cannot be measured in the blood.[10] The fact that an antigen-antibody reaction is responsible for the rejection of homografted tissue and that this response can be modified is suggested by work in which successful skin transplants were made after acquired tolerance to donor tissue resulting from the injection of donor cells into the embryonic recipient.[1] This acquired tolerance by the embryo to foreign cells probably accounts also for the survival of renal homotransplants between dizygotic bovine twins. In the human the role of acquired antibodies is suggested by recent reports of the successful homotransplantation of skin to a recipient with agammaglobulinemia.[11]

Although at the present time permanently successful renal homografts between humans cannot be performed because of this "antigen antibody like" reaction between donor tissue and recipient, skin homografts are known to survive between identical twins.[4] Having established this fact, there were several experimental observations that made the success of a renal homograft seem likely if performed between identical twins and that justified the removal of a normal kidney from a healthy donor.

First, immunologic and genetic similarity accounts for the permanent survival of skin homografts between identical twins.[4] Second, when skin or kidney homografts are carried out between antigenically dissimilar humans, the early function and the histological picture of rejection of each appears similar.[12] Third, skin and kidney homografts possess a common antigen that can sensitize a recipient to a subsequent homograft of either tissue from the same donor.[13] This further suggests that skin and kidney homografts behave similarly. Fourth, we have established to our own satisfaction that renal autografts have normal function indefinitely in animals.[14] This observation is important because, presupposing initial success of the transplant between antigenically similar (identical) twins, a second problem to be weighed was the permanency of such function. There were no reported instances of adequate functional studies in long-term surviving renal autografts.

It thus became imperative to establish beyond a reasonable doubt the fact that the twins were monozygotic (identical). Information that there was a common placenta was obtained from the hospital record of their birth. Blood samples from both twins were tested for all presently known reliable blood groups. These were found to be identical in both instances for each group (table). The two other siblings tested did not match. This was considered good but not indubitable evidence that the twins were identical. The twins and two other siblings were studied by Dr. Arthur G. Steinberg, geneticist of the Children's Medical Center, Boston, who felt that, "On the basis of eight blood group systems plus the ability to taste phenylthiocarbamide, the sex similarity, and the a priori probability of dizygotic versus monozygotic twinning, the probability that these boys are identical twins is 0.985. Other data indicating that they are identical are 1) the presence of a single placenta, 2) both twins have the relatively rare Darwin's tubercle on their ears while their sibs do not, 3) the twins have identical eye colors, including iris structure and pigment patterns, and their eyes are markedly different from their sibs' eyes in color and in iris structure, 4) there are no data suggesting they are not identical. My conclusion is that the twins are identical." Final decision to operate, however, was based on the most closely applicable evidence for antigenic similarity, that is the survival of transplanted skin between the two twins (fig. 1).

Evaluation of several factors determined the site for transplantation. The natural site for the homograft, the renal fossa, has two disadvantages. First, it requires simultaneous nephrectomy, thus increasing the magnitude of the operation. Secondly, it necessitates a ureteroureteral anastomosis with the possibility of subsequent stricture formation because the length of the transplanted ureter vascularized by the renal pedicle is too short to reach the bladder. The upper thigh, the site of 13 previous homotransplants, was not used because it requires a skin ureterostomy with the possibility of subsequent ascending infection. In addition, it creates a problem in the collection of urine.[5] The site selected, utilizing the iliac vessels for an anastomosis and placing the homograft retroperitoneally within the pelvis, allows implantation of the short ureteral segment directly into the bladder and places the kidney in its natural thermal environment. Furthermore, gravity drainage of the renal pelvis and ureter approaches normal physiological con-

6. Sterling, J. A., and Goldsmith, R.: Total Transplantation of the Thyroid Using Vascular Anastomosis: Report of a Successful Result in Chronic Tetany, Surgery **35**: 624, 1954.

7. Gaillard, P. J.: Transplantation of Cultivated Parathyroid Gland Tissue in Man, in Preservation and Transplantation of Normal Tissues, Ciba Foundation Symposium, edited by G. E. W. Wolstenholme and M. P. Cameron, London, J. & A. Churchill, Ltd., 1954, pp. 100-109.

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9. Maumenee, A. E.: The Immune Concept: Its Relation to Corneal Homotransplantation, Ann. New York Acad. Sc. **59**: 453, 1955.

10. Pressman, D.: Tissue Localizing Antibodies, Ann. New York Acad. Sc. **59**: 376, 1955.

11. Good, R. A., and Varco, R. L.: Successful Homograft of Skin in a Child with Agammaglobulinemia: Studies in Agammaglobulinemia, J. A. M. A. **157**: 713 (Feb. 26) 1955.

12. Dempster, W. J.: Problems Involved in the Homotransplantation of Tissues, with Particular Reference to Skin, Brit. M. J. **2**: 1041, 1951.

13. Simonsen, M., and others: Biological Incompatibility in Kidney Transplantation in Dogs: Experimental and Morphological Investigations, Acta path et microbiol. scandinav. **32**: 1, 1953.

14. Murray, J. E.; Lang, S.; Miller, B. F., and Dammin, G.: Long Term Functional Studies on Autotransplanted Kidneys in Dogs: unpublished data.

ditions. The observations mentioned above, that renal autografts in animals maintain normal function indefinitely, appear important because of the previous opinion of other investigators that renal autografts so capable of survival soon develop impaired function manifested by abnormal renal dynamics and electrolyte excretion.[15] We surmised that the permanently successful function ob-

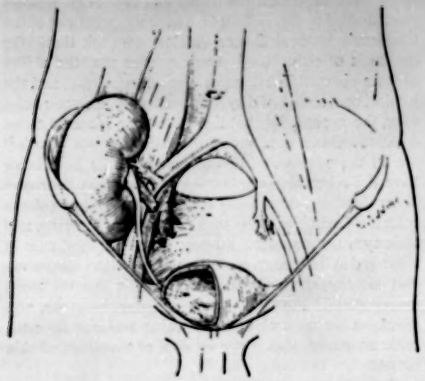


Fig. 2.—Schematic diagram of renal homograft in situ showing vascular anastomoses completed and ureter implanted in bladder. Renal artery end-to-end with hypogastric; renal vein end-to-side with common iliac; ureter mucosa-to-mucosa anastomosis with bladder.

served in our animal experiments resulted from the use of a recipient site that allows direct implantation of the ureter into the bladder, which has a normal thermal environment and which allows gravity drainage. This laboratory technique proved adaptable for use in man, provided that the left kidney was placed into the right iliac area or the right kidney into the left iliac fossa, thus reversing the normal anteroposterior relationship of the artery, vein, and ureter.

With this background, a nephrectomy was begun on the donor simultaneously with the operation on the recipient in an adjacent operating room. Through a right lower quadrant incision, the retroperitoneal area was entered exposing the right iliac vessels in the recipient. The operation was begun at 8:15 a. m., and the vessels were prepared for the anastomoses by 9:50 a. m. The donor kidney was brought into the room at 9:53 a. m. At this time the common iliac artery was occluded for the duration of the anastomosis. An end-to-end anastomosis between the free end of the hypogastric artery and the renal artery was completed at 10:40 a. m., and an end-to-side anastomosis between the renal vein and the common iliac vein was finished at 11:15 a. m. Total ischemia of the donor kidney was one hour and 22 minutes. Both arterial and venous anastomoses were satisfactory, and the entire kidney became turgid and pink immediately on release of the arterial clamp. Therefore, a small artery in the renal pedicle that appeared to be an accessory renal artery was ligated rather than anastomosed. The last clamp was removed from the common iliac artery 10 minutes later, and pulsation was noted in the right foot immediately. At this point a suprapubic cystotomy was made in the medial and superior portion of the bladder and a small tunnel dissected in the submucosa. The ureter was let in through the muscular wall of the bladder and through the submucosal tunnel, and a mucosa-to-mucosa suture was carried out (fig. 2). A polyethylene ureteral catheter had been inserted in the ureter to the renal pelvis and carried out through the cystotomy at this time. The incisions in the bladder were then closed after a mushroom catheter had been inserted from a suprapubic site. At this time clear urine was flowing copiously from the ureteral catheter. The kidney now lay rather neatly in its new site except that it projected forward where the lower pole impinged upon the iliac crest. The kidney was fixed by sutures to prevent its rotation, and the overlying oblique muscles and fascia were sutured together over it. The total operating time was three hours and 30 minutes. The postoperative course was smooth, and the incision healed per primam. The ureteral catheter was removed on the ninth postoperative day after evidence of function had been confirmed by the prompt excretion of injected sodium indigotindisulfonate.

The patient's subsequent course was characterized by continued improvement. Renal function improved; and, as it did so, acidosis and nitrogen retention disappeared (fig. 3). There was a marked decrease in blood pres-

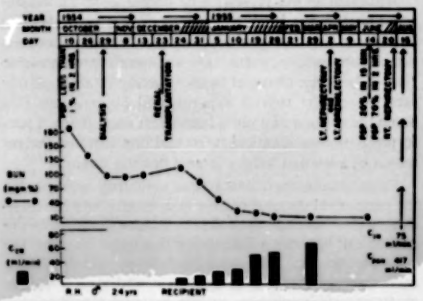


Fig. 3.—Disappearance of azotemia and improvement in renal function after renal homotransplantation. There is a progressive decrease in blood urea nitrogen and an increase in serial creatinine clearances (shown in solid bars at the bottom of the diagram). In October, 1954, there was almost no discernible phenolsulfonphthalein excretion. On June 14, 1955, phenolsulfonphthalein excretion was normal. In August, 1955, filtration rate and renal plasma flow as measured by the clearances of inulin and *p*-aminohippurate were at near normal values.

sure, and with this decrease the evidence of cardiovascular disease disappeared (fig. 4). Marked cardiomegaly (fig. 5) disappeared, and the abnormalities in the electrocardiogram vanished. The significance of these changes by the addition of a normally functioning kidney in the presence of two badly damaged kidneys will be discussed in a future publication.[16]

15. Dempster, W. J., and Jorkes, A. M.: Diuresis and Antidiuresis in Kidneys Autotransplanted to the Neck of Dogs, Quart. J. Exper. Physiol. **38**: 11, 1953.

16. Merrill, J. P.; Guild, W. R., and Reardan, J. B.: Observations on Renal Hypertension in the Human Following Bilateral Nephrectomy and Successful Renal Homotransplantation: unpublished data.

During the follow-up visits, however, the patient continued to show evidence of some elevation of blood pressure. This elevation was labile and in some instances directly related to the presence of the examining physician. A persistent tachycardia (pulse rate of 90 to 100 per minute) continued in spite of normal blood chemistry and hemoglobin values. The urine continued to show 6 to 8 white blood cells, a rare cast, and 1+ protein. Clean voided urine specimens grew out a variety of organisms, which included P. vulgaris and Esch. coli. In vitro sensitivity tests showed these organisms to be resistent to most of the antibiotics except chloramphenicol. Colony counts varied from 100 colonies per milliliter on a pour plate to 2,000 colonies. After a consideration of the foregoing facts, it was decided to remove the two damaged kidneys for the following reasons. 1. Intravenous pyelography and renal function tests had shown that the renal homograft was functioning well. 2. The data indicated almost total lack of function in the two diseased kidneys. 3. The possibility existed that infection of the graft might occur from the two remaining diseased kidneys. 4. Experimental evidence suggests that a nonfunctioning or infected kidney may ultimately interfere with the function of a normal kidney, particularly with regard to its role in preventing renal hypertension.

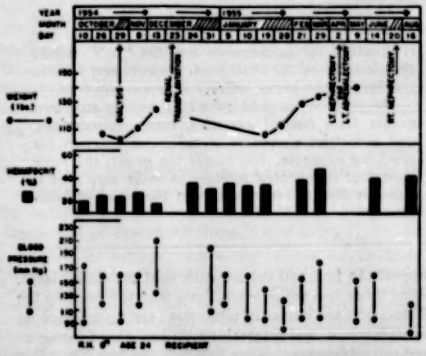


Fig. 4.—There is striking decrease in blood pressure immediately after renal transplantation and some tendency for this to rise again with improved levels after left nephrectomy and return to normal values after removal of the second diseased kidney. Increase in hematocrit and gain in weight reflect improvement in general clinical condition.

After the second nephrectomy the patient's blood pressure stabilized at lower, and almost normal, levels. Frequent urine examinations since that time have shown clearing of the evidence of urinary tract infection. Some proteinuria, however, persists. The renal function of the homograft as measured by the clearance of inulin and *p*-aminohippurate closely approximates that of its fellow, which remains in the donor twin. Intravenous urography shows prompt excretion of dye in good concentration (fig. 6). The ureter appears somewhat dilated and tortuous, but this appearance might be expected in view of the fact that it lacks innervation.

The survival of the renal homograft for this period of time with continuing good function indicates the complete lack of a rejection response by the host and demonstrates that renal transplantation is a technically feasible procedure. It stresses further that, as indicated in previous studies,[3] total anoxia of the kidney (in this case for a period of one hour and a half) does not mitigate against resumption of adequate function. The implications of the dramatic response in malignant hypertensive disease to the transplantation of a normal kidney should carry considerable weight in future thinking about the renal mechanism in human hypertension. Why one identical twin and not the other should develop glomerulonephritis and whether the kidney of the unaffected twin transplanted into the diseased recipient will be susceptible to further attacks is a question still to be answered. Unanswered also is the question of whether the transplanted kidney in its unusual position with a short and abnormally innervated ureter will escape eventual infection.

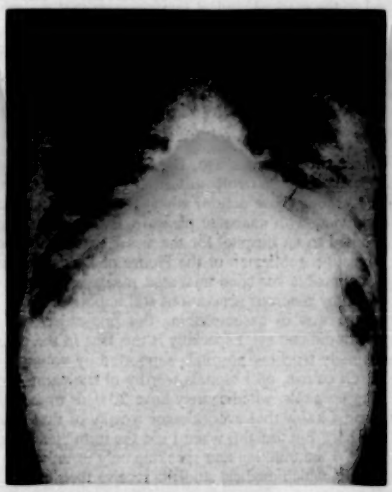


Fig. 5.—Chest film taken nine days before operation shows marked cardiomegaly and pulmonary congestion. Three weeks after operation lung fields were clear and heart size decreased to within normal limits.

Fig. 6.—There is prompt excretion of the opaque medium in good concentration. Renal pelvis shows no extrarenal dilatation but there is definite dilatation of ureter, attributed to complete denervation of the kidney. No evidence of ureterovesicle obstruction is seen and prompt emptying of ureter into bladder occurs. Bladder is seen to be partially filled on this exposure and more so on subsequent exposures.

SUMMARY

Homotransplantation of a healthy kidney from one identical twin to another was performed. The homograft has survived for a 12-month period, and renal function is apparently normal despite the fact that both of the recipient's diseased kidneys were removed. A striking sequel to the marked clinical improvement that was observed was the disappearance of the signs of malignant hypertension. Tissue transplantation including that of a functioning kidney appears to be a feasible procedure in identical twins, but to date successful permanently functioning homografts appear to be limited to such individuals.

721 Huntington Ave. (15) (Dr. Merrill).

LET'S SAVE THE GOOSE THAT LAYS THE GOLDEN EGGS

Robert Cutler, LL.D. (Hon.), Boston

• The university hospitals in which medical students receive their clinical training house a matchless spirit of research, and their valuable facilities must be preserved to work for the generations to come. At present they are caught between fast-rising operating costs and diminishing collectible charges to patients.

An important difficulty arises from the difference between the "hard" money that pays overhead and is essential for permanence and the "soft" money that is received for short-term projects and fails to provide for the heavy indirect expenses involved.

The problem must be solved by making sure that grants from federal agencies, funds, foundations, and industries apportion a sufficient fraction for overhead expenses. The larger the grant, the more important is repeated scrutiny to make sure that it does not threaten the stability of the recipient institution.

Almost two centuries ago, Dr. Samuel Johnson, the great lexicographer wrote this in his broadsheet, the Idler: "Among those actions which the mind can most securely view with unabated pleasure, is that of having contributed to an hospital for the sick." [1] It should be our objective, gentlemen of the House of Delegates, to make it possible for such unabated pleasure to be experienced by generous generations still unborn.

But the way of accomplishing this fine objective is beset with difficulties. Especially is this true in the case of university teaching hospitals supported by voluntary funds. Of course, all hospitals worthy of the name are teaching hospitals, whether they have 20 beds or 2,000 beds, and I know that every doctor worthy of that title is a teacher. But tonight, when I use the term "teaching hospital," I am thinking and speaking only of university hospitals in which medical students receive their clinical training.

Let us get down to brass tacks. The fact is that our voluntarily supported hospitals are caught in the Big Squeeze. They are caught in that shrinking space between the upper millstone of collectible charges to patients and the nether millstone of skyrocketing operating costs. Sometimes it seems as if every hand were against the viability of voluntary hospitals. The legislature passes each year one or more laws that increase our burdens. The economic cycle pushes up the cost of services, of food, of supplies. And then our best friends, the doctors, keep on discovering and inventing new wonder-drugs, new mechanisms, new necessities for the saving of human life. Upon the university teaching hospitals of America a new burden has come crushing down since World War II. This burden, the child of increased research activities and increased costs related thereto, is what I want to talk about to you tonight.

COSTS OF RESEARCH

My own hospital, the Peter Bent Brigham, is a relatively small (280 bed) general hospital affiliated with the Harvard Medical School and forming an integral part of what we call the Harvard Medical Centre. The Brigham's professional staff is shared with the Harvard Medical School. The Brigham Hospital has three functions: One is to care for the sick; the other two buttress and support the first and suffuse with light the dark places. These other two are to teach those who will become the doctors and the nurses of tomorrow, and to advance by exact, inspired, and researching skill mankind's store of medical knowledge.

As a trustee, I sometimes seem to alarm my great professors with my consciousness of the cost of research. But they really know better. Beyond any shadow of doubt, I march under the banner of inquiring research. In a university hospital, research is the pulsing arterial blood of life. It is the vital essence, as important to such a hospital's place in the scheme of things as breath is to the nostrils of a living man. And I glory, as a lay brother, in the accomplishments of America's teaching hospitals. To salute what they have achieved is not intended to, and does not in any way, derogate from the solid achievements of our other great hospitals. In this work, it is easy to find enough stars for everyone's crown.

But I do say that the voluntarily supported university teaching institutions are, by their performance, a frontline in America's care for the sick, today and tomorrow. Here are the geese that have been laying the golden eggs of medical discovery, and it is of primary consequence to the progress of medicine that these precious birds be assured in the years ahead of every opportunity for reproduction and for lying-in.

One of the difficulties confronting voluntarily supported medical schools and their affiliated hospitals to

Chairman of the Board of Trustees of Peter Bent Brigham Hospital and Chairman of the Harvard University Board of Overseers' Committee to Visit the Harvard Medical and Dental Schools.

Read at the Dinner for House of Delegates, Ninth Clinical Meeting of American Medical Association, Boston, Nov. 30, 1955.

1. The Idler, no. 4, May 6, 1758.

which I earlier referred is the magnitude of cost to the school or the hospital of the research activities that it now carries on. President Conant, in his 1950-1951 Annual Report for Harvard University, had this to say of the broad implications of expanding research expenditures:

> There are limits to the amount of temporary money that should be expended by any department of the University. No blanket rule can be laid down, but clearly permanent appointments in any area financed by temporary grants are in reality a liability against the unrestricted income from endowment of the entire University—an amount that represents but a small fraction of our annual income. Furthermore, commitments may become permanent in a university without any official action—moral commitments are so readily developed to this or that enterprise. Every proposal for expansion must be scrutinized with great care, therefore, to see whether or not it places in jeopardy our permanent resources. Many a worth-while project supported by only a five-year grant or annual giving must be refused.

These words were written at a time when federal expenditures for research and development in all fields totaled only 1.3 billion dollars a year. In fiscal year 1954, the last full year I was in Washington, the federal government alone was expending about 2.2 billion dollars on such research and development. This golden outpouring flows also from foundations, from trusts, from industry, from individuals, and from funds raised annually to combat specific ills, such as cancer, heart disease, and poliomyelitis.

What are some consequences of this shining inundation? In the annual report that I rendered recently to the Board of Overseers of Harvard College, as chairman of the Board's Committee to visit the Medical School and the School of Dental Medicine, I said this:

> In 1910, the School's "hard money" income was ten times its "soft money" grants and gifts; in 1954, the "soft money" exceeded the "hard money." More and more, as time goes by, the School is forced to carry on its high calling upon a foundation of sand which may shift away. There is no assurance that these governmental and other research grants—with their inadequate provision for "overhead"—will continue their support through the long look ahead.

Let me repeat. In fiscal year 1954 the Harvard Medical School expended more from gifts and grants from outside sources (what we call "soft money") than it received from students, from endowment funds, and from other university sources (what we call "hard money"). This great largesse of research funds is a heady wine. As Dr. Conant said, the very size of this research money requires that each project be scrutinized over and over again with great care, not only to determine its individual merit but also to be sure that its acceptance will not throw us out-of-balance and place in jeopardy our permanent resources.

OVERHEAD EXPENSES RELATED TO RESEARCH GRANTS

But let me descend from this upper plateau of educational policy to the rocky lowland of fiscal reality, upon which first breaks the incoming tide of research money. In my report to the Harvard Overseers, I made reference to the inadequate provision in research grants and contracts for overhead or indirect expense.

Now, this item of unreimbursed overhead expense in relation to research grants is Peck's Bad Boy. It is of this unseen, but omnipresent, fellow that I want especially to speak.

The crucial nature of this problem is revealed by looking at the expenditures for research made in a particular year by the Harvard Medical School and its affiliated voluntarily supported hospitals, the complex that we call the Harvard Medical Centre. In fiscal year 1954 there was expended from funds that had been given to the members of this complex for research a total of $5,130,000. Fairly computed, the overhead charge attributable to this great sum came to over $1,500,000. But those who had provided so great a sum for direct research expenses had provided only $513,000 for indirect expenses. Accordingly, about a million dollars that year had to be taken from the strained general funds of the members of the Harvard Medical Centre.

Look for a moment at Brigham Hospital, one member of the Harvard Medical Centre, and how it fared in the same year. From funds given to it or to the Medical School for research projects to be carried on within the hospital, there was expended on direct costs of these research projects more than $700,000. Overhead or indirect expense related to these direct expenditures approximated $235,000. If we include in such overhead only out-of-pocket expense, and make a contribution of use of facilities, the figure comes to $190,000. However, the grantors of the research funds provided toward overhead only about $51,000. Thus, there resulted an overhead deficit of some $140,000. The cash to meet this deficit came from the general funds of the hospital and the school, thereby further diminishing for the next year their "hard money" endowment income.

This is the way to kill the goose that lays the golden eggs. This is the way to commit "medical research suicide," with both your eyes open. What I am talking about is not a frill or a trifle. I am talking of the central supply of blood to the heart of medical research. A million dollars a year in unreimbursed research overhead at just one medical teaching complex! In the American vernacular, "that ain't hay."

This situation prompted Dean George Berry to write,[2] as follows:

> An additional burden is the portion of . . . (the School's hard money income) required to meet a large share of the indirect costs of research in a total program that grows more complex by the day. This leads me to ask what others have been asking too: Has the Medical School reached the point of saturation on research? In a certain sense, it has. So many of the School's fiscal problems already relate to the large total of research grants that I can only speculate on the possible arrival of the day, perhaps not too far distant, when the School's entire research structure will have to be drastically overhauled. . . .
>
> (Yet) there can be no progress in medicine without research. Research and teaching must go hand in hand. The issue is to find out how to make research interlock more effectively with teaching to the end that the whole will be stronger than the parts. In the last analysis, the problem is to devise the way to make ourselves able better to afford our large research activities.

SOLVING THE PROBLEM

There is a "way to make ourselves able better to afford our large research activities." Several years ago Harvard University retained the best accounting brains it

2. Berry, G.: Financing the Harvard Medical School, Harvard M. Alumni Bull., April, 1955.

could find to devise sound methods of computing the direct and indirect (or overhead) expenses of each of its component departments and institutions. The accountants' report furnished to the Harvard Medical School and to each of its affiliated hospitals a formula that, when applied to a research grant or contract, would give the percentage of overhead expense related thereto. This formula is simple in concept. It proceeds on the familiar basis that the three principal factors in computing indirect expense are administration and general expense, operation and maintenance, and use charges or depreciation.

The Boston institutions have been making computations based on this formula for several years. Today each element of the Harvard Medical Centre knows exactly what its overhead expense is, in detail and in total. Today, we are well equipped to place research operations on a hard basis of fiscal fact and remove them from the preexisting area of speculation. We are in a documented position to demonstrate to those who provide research funds just what indirect expense reimbursement should be furnished if our institutions are to be able to carry on in the years ahead. And we shall try to stand together in carrying out such a sensible and prudent policy, which will work for the good of all and the good of each.

For some time now, the policy of the Defense Department and its component services, and latterly the policy of the Atomic Energy Commission, has been to pay to the recipients of their research funds an amount for overhead expense computed according to these same accounting principles. The application of these principles is a realistic approach that should be generally acceptable to all.

In the spring of 1955, a special committee appointed by the National Science Foundation to study for the federal government this overhead expense reimbursement problem filed its report. The special committee recommended that the federal government adopt in the future an over-all policy relating to reimbursement of overhead expense to grantees and contractees of federal research funds. This new policy would offer to recipients full or substantially full reimbursement for indirect expenses on the basis of sound accounting principals. This sound and farsighted recommendation was hailed by those of us who have been laboring in this field for the common good. Leaders in the Eisenhower administration have shown sympathetic appreciation of its validity. We earnestly hope that the federal government will adopt such a policy as part of its next fiscal year budget. Those of us who can are doing more than hope: we are telling the story in every ear at every chance.

Adoption by the federal government of the recommended realistic policy for reimbursement of overhead expense would have two beneficial effects. The National Science Foundation and the Public Health Service, now reimbursing 15% for overhead expense, would raise their standards to those already in effect at the Pentagon and at the Atomic Energy Commission. And the pattern thus uniformly set for federal grants could be expected to have a deep impression upon foundation, fund, and industry grantors. Some of these latter givers already sincerely understand that teaching institutions, like a fagged-out horse, cannot run the victorious race if made to carry too large a burden of indirect research costs.

I venture to say that no single act by the federal government could mean more and give more hope to the teaching institutions in connection with their medical research activities than federal adoption of such a realistic general policy for reimbursing overhead expense. With this guiding light to follow, all of us who have responsibilities in this area would be encouraged and better able to spread a gospel to all nongovernment grantors of research funds. Working together in a realistic educational crusade, we should surely attain a goal of stronger research programs in stronger institutions.

Let me add a point that I have made to persons in high authority in the Eisenhower administration. I believe sincerely that, in a free democracy such as ours, the grantor and grantee in a research project should be "partners." My hospital does not ask that it be reimbursed for its total overhead expense. We wish to share in the project, over and above our contributing the high skills of our professional staff. To that end, we are willing to give so much of our overhead expense as is within our means. And the trustees of the Brigham Hospital have now adopted as policy a declaration to this effect.

STRONGER TOMORROW THAN TODAY

I ask each of you to consider and understand this critical situation in medical research and medical education. Will each of you join as an evangel to the givers, grantors, and contractors, public and private, of research funds, to tell of the need to place reimbursement for research overhead expense on the realistic basis that I have described? If you will, you will be helping to make American medicine even stronger tomorrow than it is today.

Many people are accustomed to believe only what they feel or see. The doctor does not feel or see the overhead expense, but we trustees do. This villain is not hidden from us. He turns up every night in the treasurer's office to devour our "hard money" resources. For me, at least, research will have its "golden age" when the grantors and contractors who provide for direct expenditures will as equitably and realistically provide for indirect expenditures. Then, indeed, our medical research goose will be able to continue, for time untold, to lay the golden eggs of discovery.

All of us want the same thing. We want to make the sick well. We want to push back the frontiers of medical knowledge. We want a bubbling fountain of medical research. We want America's voluntarily supported institutions, tried and precious mechanisms for the advancement of knowledge, to thrive on in the future as in the past. We can better have these things if those institutions that carry the heavy load of medical research undertakings are enabled to do so on a basis that is realistic under existing circumstances and that takes into account their slender capacities to pay. For, in this way, their matchless spirit and their valuable facilities will be preserved to work for the generations that are still to come.

CLINICAL NOTES

PORTABLE TELEPHONE AMPLIFIER

Matthew N. Hosmer, M.D., San Francisco

There has long been a need for a device that would allow the hard-of-hearing patient to use any telephone anytime and place without inconvenience or embarrassment, and I believe a new portable telephone amplifier called the "Phone-Aid" is the answer. It is a pocket-sized amplifier, weighing about 3 oz., which can be easily clipped to any telephone receiver in a moment. The case is molded from a very durable shock-resistant plastic, and its design is so compact and thin that it readily fits the receiver in a manner that does not disturb the normal relation of the mouth to the transmitter.

The amplification is accomplished by an ingenious printed circuit powered by two small batteries and three hermetically sealed transistors. This increases the acoustic output of the telephone by approximately 49 db., thereby providing sufficient amplification for the majority of patients who are obliged to wear hearing aids. With this amplifier it is no longer necessary for the patient to hold the receiver against his own hearing aid, as he can now hold the receiver plus the amplifier to his ear in the normal manner.

Scottie Phone-Aid.

The pick-up of speech from the telephone is through an induction circuit located in the small arm that serves to clip the instrument to the receiver. This method serves to cut out all room noises and also eliminates noises that are caused by magnetic disturbances. The batteries usually last about 120 hours and are easily changed when they are worn out by simply removing the back plate of the instrument.

Tests conducted on a number of hard-of-hearing patients have been very successful, and it is clear from their comments that the amplifier will be found widely useful. The amplifier is called the "Scottie Phone-Aid," Scottie being the trade-mark name of the Remler Company, San Francisco, which has developed and perfected the instrument.

384 Post St.

From the subdepartment of Otolaryngology, University of California School of Medicine.

This new instrument was presented at the Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 12, 1955.

PREDNISONE (METICORTEN) IN TREATMENT OF ACQUIRED HEMOLYTIC ANEMIA

PRELIMINARY REPORT

Leon N. Sussman, M.D.
and
Jack R. Dordick, M.D., New York

The demonstration that prednisone (Meticorten) could be used as effectively in the treatment of rheumatic diseases as cortisone [1] without many of cortisone's undesirable side-effects suggested its trial in the treatment of acquired hemolytic anemia. It had been shown that corticosteroids depress the rate of hemolysis [2] or diminish the titer of antibody,[2] thus enabling the overly active erythropoiesis to reach a satisfactory equilibrium with the peripheral red blood cell count. Where long-term therapy is indicated, the elimination of sodium retention, hypertension, and diabetogenic effects of these drugs would be advantageous. The availability of prednisone in the past year has made possible the treatment of the following three cases of acquired hemolytic anemia.

REPORT OF CASES

CASE 1.—A woman, aged 24, was first seen in 1950 with the acute onset of weakness, anorexia, and anemia of one week's duration. On admission to the hospital, pallor, icterus, and splenomegaly of 4 cm. below the costal margin was noted. The blood cell count revealed the hemoglobin level to be 4.3 gm. per 100 cc.; erythrocytes 1,900,000 per cubic millimeter, with 9.4% reticulocytes; and leukocytes 9,000 per cubic millimeter, with a normal differential, except for 1% normoblasts. The serum bilirubin level was 4 mg. per 100 cc. The Coombs test and the L. E. preparation were negative. All hematological studies including the fragility test were normal. The sternal marrow aspirate revealed a markedly erythronormoblastic marrow, with a myeloid-erythroid ratio of 1:1. The patient was transfused, and several courses of cortisone and corticotropin (ACTH) were unsuccessful in maintaining the hemoglobin at a satisfactory level. Following splenectomy the laboratory findings were more satisfactory. The patient was discharged after four months with a hemoglobin level of 11.5 gm. per 100 cc., red blood cell count of 3,640,000 per cubic millimeter with 2.5% reticulocytes, and a serum bilirubin level of 0.78 mg. per 100 cc.

The patient was not seen until September, 1954, when she again appeared with complaints of weakness and anemia. At this examination the hemoglobin level was 8.5 gm. per 100 cc. and the red blood cell count was 2,500,000 per cubic millimeter, with 25% reticulocytes. Several normoblasts were seen in the peripheral blood smear. The Coombs test was found to be strongly positive. Serologic study identified the autoanti-

From the Medical Service and Hematology Laboratory of Beth Israel Hospital.

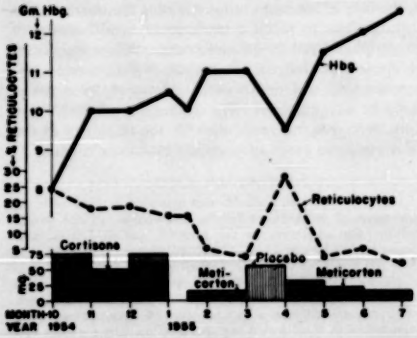
The prednisone used in this study was supplied as Meticorten by the Schering Corporation, Bloomfield, N. J.

1. (a) Dordick, J. R., and Gluck, E. J.: Preliminary Clinical Trials with Prednisone (Meticorten) in Rheumatic Diseases, J. A. M. A. **158**: 166 (May 21) 1955. (b) Bunim, J. J.; Pechet, M. M., and Bollet, A. J.: Studies on Metacortandralone and Metacortandracin in Rheumatoid Arthritis, ibid. **157**: 311 (Jan. 22) 1955.

2. Dacie, J. V.: The Hæmolytic Anæmias, London, J. & A. Churchill, Ltd., 1954, pp. 317-327.

3. Damashek, W.; Rosenthal, M. C., and Schwartz, L. I.: The Treatment of Acquired Hemolytic Anemia with Adrenocorticotrophic Hormone (ACTH), New England J. Med. **244**: 117 (Jan. 25) 1951.

body to be of specificity anti-rh"(E).[4] Therapy was begun with cortisone, 25 mg. three times a day, and continued for three weeks, at which time a maximum improvement seemed to have been reached. The blood cell count showed 10 gm. of hemoglobin per 100 cc. and red blood cell count of 3 million per cubic millimeter, with reticulocytes 18%. The serum bilirubin level was 2.6 mg. per 100 cc., of which 0.3 mg. was direct. Medication was discontinued for one month, and then therapy with prednisone (Meticorten) in the dosage of 5 mg. three times a day was started. One month later blood chemistry studies showed the hemoglobin level to be 11 gm. per 100 cc.; red blood cell count 4,300,000 per cubic millimeter, with 5% reticulocytes; and serum bilirubin level 3.1 mg. per 100 cc., of which 0.6 mg. was direct. At this point the prednisone was replaced with placebo. Within one month the hemoglobin level had fallen to 9.5 gm. per 100 cc. and the red blood cell count was 3 million per cubic millimeter, with 28% reticulocytes. The patient again complained of weakness, fatigue, and anorexia. Prednisone therapy was restarted in doses of 10 mg. three times a day, with a prompt improvement in all symptoms. After a month the dose was reduced to 5 mg. three times a day. At this time the hemoglobin level was 13 gm. per 100 cc. and red blood cell count 4 million per cubic millimeter, with only 1% reticulocytes. The serum bilirubin level was 2.6 mg. per 100 cc., with only 0.35 mg. being direct. The Coombs test remained strongly positive.



Hemoglobin and reticulocyte response to therapy in patient in case 1.

During the period of prednisone administration, weekly electrolyte studies of the blood for sodium, potassium, chloride, and carbon dioxide, as well as total protein, albumin-globulin ratio, and 24 hour urine excretion studies were consistently normal. The patient's diet has been unrestricted. No adverse side-effects such as edema, glycosuria, or hypertension were seen. The patient at present has continued on a regimen of 5 mg. of prednisone three times a day. She volunteered the information that she "never felt better in my life" (see figure).

Case 2.—A woman, aged 57, was seen in 1951, at which time a diagnosis of lymphosarcoma of the lacrimal gland was made after biopsy. One year later, a laparotomy for pelvic mass revealed the same pathological diagnosis. With intensive x-ray therapy, all signs of the disease disappeared. The patient remained well until two weeks prior to admission in 1955, when she developed fever, cough, and weakness. A diagnosis of viral pneumonia was made by her local physician, and the patient was referred to the hospital. The physical examination at that time revealed icterus and splenomegaly of 4 cm. below the costal margin. The lungs by physical and roentgen examination were normal. Hematological studies revealed the hemoglobin level to be 4.2 gm. per 100 cc. and the erythrocytes to be 1,950,000 per cubic millimeter, with 20% reticulocytes. The serum bilirubin level was 3.6 mg. per 100 cc., with 0.5 mg. being direct. The Coombs test at 37 C was only slightly positive, whereas at 4 C this test was strongly positive. Serologic study revealed the presence of a cold panagglutinin with a titer of 1:1,800 at 4 C, 1:40 at 20 C, and only 1:10 at 37 C. Transfusions could be successfully performed with prewarmed blood (at 37 C) and slow administration. To control the patient's autohemolysis, cortisone, 100 mg. three times a day, was given. In view of the previous pathological diagnosis of lymphosarcoma, a course of x-ray therapy was directed to the enlarged spleen. The improvement in the patient's physical condition was remarkable, although serologically the titer of the cold agglutinin showed no change. After one month of therapy, when the hemoglobin level was 11.8 gm. per 100 cc. and the reticulocyte count only 1%, the cortisone was gradually withdrawn. The possibility of the cold agglutinin being part of the suspected atypical pneumonia and not related to the primary disease was considered in taking this step. However, there was a prompt fall in hemoglobin level to 5.7 gm., with a slight rise in reticulocytes and serum bilirubin level and the prompt recurrence of all the original symptoms. The sternal marrow aspirate at this time revealed a markedly erythroblastic marrow with many macrocytes. The failure of reticulocytosis to appear in the peripheral blood in proportion to the intense erythroblastic activity in the marrow suggested the additional element of nutritional maturation arrest. After several transfusions and the administration of folic acid, 5 mg. three times a day, the expected reticulocytosis appeared. Administration of prednisone, 10 mg. three times a day, resulted in a sustained hemoglobin level of 10.8 gm. per 100 cc., with 1.2% reticulocytes, and a fall in serum bilirubin level. The prednisone dosage was then reduced to 5 mg. three times a day. The patient's condition is now satisfactorily maintained at this dosage.

Case 3.—A 71-year-old woman had been under observation for chronic lymphatic leukemia and cardiac decompensation. She rather abruptly developed a severe anemia, icterus, weakness, and dyspnea. This sudden change in her condition was accompanied by a positive direct Coombs test, bilirubinemia, and 31% reticulocytes. Her hemoglobin level was found to be 4.2 gm. per 100 cc., erythrocytes numbered 1,130,000 per cubic millimeter, and leukocytes were 342,000 per cubic millimeter, with 90% of the cells being mature lymphocytes. The serum bilirubin level was 5.8 mg. per 100 cc., with 0.63 mg. being direct. With transfusions and orally given cortisone (200 mg. daily) her condition improved, and after three weeks she was discharged with a hemoglobin level of 9 gm. per 100 cc., red blood cell count 3,030,000 per cubic millimeter, reticulocytes 4.9%, and serum bilirubin level only 0.88 mg. per 100 cc. Cortisone therapy was discontinued. Several months later her condition had deteriorated slightly. The blood cell count showed a hemoglobin level of 8.5 gm. per 100 cc. and 2,650,000 erythrocytes per cubic millimeter, with 5.8% reticulocytes. Three months later the patient was again in serious difficulty with active hemolysis. Her hemoglobin level was 5 gm., with 20% reticulocytes. At this time therapy with hydrocortisone, 10 mg. three times a day, was begun, but several transfusions were necessary in order to maintain the hemoglobin level at 8 gm. per 100 cc. Subsequently the patient was placed on therapy with prednisone, 5 mg. four times a day. For several months her hemoglobin level has been maintained at 9 gm. per 100 cc., with red blood count 3,500,000 per cubic millimeter and reticulocytes only 4%. Continual therapy over a long period has not resulted in any increase in cardiac decompensation, edema, or other evidence of fluid retention. This patient is maintained on a salt-poor diet because of her cardiac status, and she is comfortable and active. The effectiveness of small doses of prednisone in controlling the hemolytic state when cardiac decompensation would be a deterrent to the use of other corticosteroids constitutes a therapeutic advance in the treatment of this combination of diseases.

COMMENT

The satisfactory remission of acute hemolytic anemia obtained by the use of prednisone in relatively small dosage occurred without the appearance of any undesirable side-effects. No alterations in the levels of serum sodium, potassium, chlorides, bicarbonate, or plasma

4. Sussman, L. N., and Pretshold, H.: Elution Technic for the Identification of Antibody-Coated Erythrocytes, Am. J. Clin. Path. 24:1430 (Dec.) 1954.

proteins were noted. No edema, hypertension, or gain in weight was seen. No dietary sodium intake restrictions were applied, except where indicated for other conditions, as in the patient in case 3, who had cardiac decompensation. No abnormal variations in urinary electrolytes were evident. In this series no evidence of diabetogenic activity was apparent. It would seem likely that in a larger series there would appear instances of epigastric distress as reported by Dordick,[18] euphorogenic effects, and probably some evidence of undesirable metabolic activity. However, the effectiveness of this preparation in the small dosage utilized makes its further study essential.

CONCLUSIONS

Prednisone (Meticorten) was administered to three patients with acute hemolytic anemia due to an acquired autoantibody. In this preliminary series an effective control of the hemolytic process was obtained with small doses of the medicament. Although similar effects have been obtained with other steroids, the relative freedom of use of prednisone from significant metabolic and electrolytic disturbance makes it a desirable drug in the treatment of acute hemolytic anemia.

36 E. 38th St. (16) (Dr. Sussman).

COUNCIL ON PHARMACY AND CHEMISTRY

Report to the Council

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary.*

In July, 1954, the Subcommittee on Blood Dyscrasias established a registry in the headquarters office of the Committee on Research for the reporting of blood dyscrasias caused by toxic agents. Since that time, 33 cooperating hematologists have reported 110 cases of blood dyscrasia that they considered to be caused by various drugs and toxic chemicals. A review of this series revealed that nine of the cases reported were associated with the use of the new drug chlorpromazine. Since the main purpose of the registry is to warn physicians at the earliest possible moment of the occurrence of blood dyscrasias coincident with the use of newly introduced drugs, it was felt important to call this fact to the attention of the medical profession.

NORMAN DE NOSAQUO, M.D., *Secretary*
Committee on Research.

BLOOD DYSCRASIAS ASSOCIATED WITH CHLORPROMAZINE THERAPY

A review of the reports received from cooperating hematologists since July, 1954, first revealed nine cases of blood dyscrasia associated with chlorpromazine therapy. A search of the literature has revealed six additional cases reported in American and British literature to the date of preparation of this report. Through the cooperation of Smith, Kline & French Laboratories, 32 other cases occurring in the United States were added, making a total of some 45 reported cases of blood dyscrasias coincident with chlorpromazine therapy. It should be emphasized that in many instances other drugs also had been given. As with reports of any such clinical association, the evidence is circumstantial rather than final but may nevertheless be significant.

Smith, Kline & French Laboratories have estimated that approximately 4 million people in the United States have been exposed to chlorpromazine since its introduction. Although it must be assumed that not all cases of blood dyscrasia associated with the drug have been reported, the indications are that the rate of incidence of blood dyscrasia is low, involving possibly only 1 in 50,000 to 100,000 patients receiving the drug (0.002 to 0.001%).

The blood dyscrasia most often reported was agranulocytosis, although in many cases bone marrow studies revealed depression of other cellular elements as well as the granulocyte precursors. In 17 patients in whom this condition appeared the outcome was fatal; however, in cases recognized early, recovery generally followed cessation of chlorpromazine administration.

Physicians who prescribe chlorpromazine should instruct their patients to report at once any sudden occurrence of sore throat or other signs of reaction. Differential blood cell counts should be done routinely; however, since the onset of this condition may be sudden and since the disease may develop fully before the patient reports to the physician, routine blood cell counts cannot be relied upon as the sole criterion for agranulocytosis. Because of this possibility the patient must be warned to be alert to any change.

Smith, Kline & French Laboratories have included this type of warning rather prominently in their literature, and they should be commended for their wholehearted cooperation with the Subcommittee. The Subcommittee suggests that, since the drug appears to possess a potential for some harm, it should be recommended that physicians limit its use to those conditions in which such use is warranted and avoid its use in the treatment of trivial or minor complaints.

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs that appear in this column have been authorized by the Council for publication and inclusion in New and Nonofficial Remedies. They are based upon the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary.*

Chlorpromazine Hydrochloride.—2-Chloro-10-(3-dimethylaminopropyl)phenothiazine hydrochloride.—The structural formula of chlorpromazine hydrochloride may be represented as follows:

Actions and Uses.—Chlorpromazine hydrochloride, one of the phenothiazine group of compounds, produces depression of the central nervous system. Generally, the electroencephalographic patterns are not altered with the usual dose in normal patients, although some variation has occasionally been reported. It suppresses or abolishes conditioned reflexes in trained rats. It also exhibits a depressant action on certain neural centers in experimental animals, resulting in suppression of vomiting from apomorphine hydrochloride, irradiation, and motion sickness, but, in animals, does not affect the emesis from morphine, veratrum alkaloids, digitalis, and copper sulfate. In addition to these main pharmacological actions, chlorpromazine hydrochloride also possesses weak adrenolytic, hypotensive, antispasmodic, hypothermic, and antihistaminic effects and is capable of potentiating the action of many other agents.

Chlorpromazine hydrochloride is effective when administered orally, intramuscularly, or intravenously. The onset of action is rapid, particularly after parenteral administration. Little is known concerning the metabolic fate of the drug in the body, although current evidence suggests the liver as a possible site of detoxication. After repeated doses, a slight amount of tolerance develops, particularly to the hypotensive and hypnotic effects.

Chlorpromazine hydrochloride has been found useful for the treatment of the nausea and vomiting associated with certain disorders including carcinomatosis, uremia, acute infections, and nitrogen-mustard therapy. Although the use of chlorpromazine hydrochloride in pregnancy for the usual "morning sickness" of the first trimester must be regarded as experimental, it may be tried for controlling hyperemesis gravidarum as a complication of pregnancy, preferably before the onset of liver damage. Its antiemetic effect has been reported as useful in radiation sickness, for the nausea and vomiting produced by certain drugs (including some antibiotics), and for the control of postanesthetic and postoperative nausea and vomiting. It has not been successful in motion sickness. Chlorpromazine hydrochloride often is successful in controlling hiccups refractory to other forms of therapy and in the treatment of status asthmaticus. The drug finds its widest use in alleviating manifestations of anxiety, tension, agitation, and of lessening motor activity in both psychoneurotics and psychotics. The latter include selected cases of schizophrenia, mania, and toxic and senile psychoses. The sedative, tranquilizing, and calming properties of the drug also make it useful as an adjunct in the treatment of certain other mental disorders and in a variety of apparently unrelated conditions where emotional stress is a complicating, or even a causative, factor. It has been used successfully in some depressions where agitation and anxiety are complications. It appears to be of no value in reducing the frequency or intensity of seizures in epilepsy.

The sedative and antiemetic actions of chlorpromazine hydrochloride have been reported to facilitate treatment in acute alcoholism. Its value in narcotic drug withdrawal is not yet established. It has been used in surgical procedures, in obstetrics, and in the treatment of severe pain, especially in cancer patients, for its tranquilizing effects. Its alleged potentiation of hypnotics, sedatives, analgesics, and anesthetics is difficult to evaluate. At the present time, therefore, all these uses should be regarded as unestablished.

Chlorpromazine hydrochloride produces a number of side-effects and toxic reactions, some of which are serious. Cases of severe and fatal blood dyscrasias, including agranulocytosis, in some instances associated with hypoplastic anemia and leukopenia, have been reported after use of this drug. It should be immediately discontinued if patients exhibit evidence of bone marrow depression; physicians should also be alert for any toxic hematopoietic effects, fever, or sore throat. Peripheral blood cell counts are indicated at the onset of such symptoms during therapy.

Jaundice occurs in a significant percentage of patients receiving chlorpromazine. It usually occurs during the first two weeks of treatment but occasionally may not be evident until some time after discontinuance of the drug. There is no correlation between the occurrence of jaundice and dose used, but administration should be promptly halted at the first indication of impending icterus and the appearance of bilirubinuria. Most cases of chlorpromazine-induced jaundice clear within a few weeks after cessation of therapy; however, until longer experience is gained and more knowledge concerning the pathogenesis of this type of jaundice is acquired, physicians are cautioned against administration of the drug to patients with either the presence or history of jaundice or liver damage.

Orthostatic hypotension is a frequent side-effect of chlorpromazine therapy, particularly after parenteral administration. The drug should be given with extreme caution to patients with arteriosclerosis, cardiovascular disease, or other conditions in which a sudden drop in blood pressure may be undesirable. When parenteral administration is to be carried out, the patient must remain in the supine position for at least one hour after the injection. When necessary, pressor agents such as phenylephrine hydrochloride or levarterenol bitartrate may be used to control hypotension. Alarming reactions with failure to respond to pressor agents have been reported from even small intravenous doses. Epinephrine should never be used for this purpose, since the adrenolytic action of chlorpromazine hydrochloride may cause epinephrine reversal.

Sedation and drowsiness, which are desired therapeutic effects in the treatment of acute anxiety and severe agitation, may become unwanted side-effects in other conditions. Other side-effects include tachycardia, hypothermia, dryness of the mouth, dermatitis, photosensitivity, nausea and vomiting, and a Parkinson-like syndrome. With the exception of the latter condition, most side-effects are usually not severe enough to warrant discontinuing the drug therapy. Because of its potentiating action with many other drugs, chlorpromazine hydrochloride should be used with caution in conjunction with other agents, particularly barbiturates, narcotics, and general anesthetics. Its use is contraindicated in comatose patients or those under the influence of large doses of alcohol or other central nervous system depressants.

Chlorpromazine hydrochloride is a potent agent with complex pharmacological actions and important toxic effects and side-reactions. Although its therapeutic

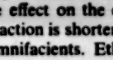
range of effectiveness is wide, sufficient experience has not been gained to determine its ultimate place in the therapeutic armamentarium. Physicians accordingly should weigh the beneficial effects to be gained against the possible toxic reactions and side-effects.

Dosage.—Chlorpromazine hydrochloride is administered orally, intramuscularly, or intravenously. The dosage must be highly individualized from patient to patient, according to the severity of the condition and the degree of response; the smallest effective dose should always be used. Oral dosage ranges from 10 to 400 mg. or more per day. Dosage for children is reduced proportionately. Deep intramuscular injection is the preferred parenteral route, with the dosage for adults ranging from 25 mg. per day for mild nausea and vomiting to as much as 400 mg. per day for acutely agitated manic patients. Because of the added danger of severe hypotension, extreme caution should be exercised in giving the drug intravenously. Because of reported instances of fatal shock, all forms of parenteral administration should usually be reserved for bedfast or hospitalized patients.

Preparations for use as stated for the foregoing drug are marketed under the following name: Thorazine Hydrochloride.

Smith, Kline & French Laboratories cooperated by furnishing scientific data to aid in the evaluation of chlorpromazine hydrochloride.

Ethinamate.—1-Ethynylcyclohexyl carbamate.—The structural formula of ethinamate may be represented as follows:



Actions and Uses.—Ethinamate is related chemically to the carbamate series of compounds, which exert only a feeble depressant effect, but it contains an ethinyl group that contributes to this action. It does not produce antipyretic, analgesic, or diuretic action, but it does exhibit a mild sedative effect on the central nervous system. Its duration of action is shorter than that produced by the barbiturate somnifacients. Ethinamate thus is useful chiefly as a hypnotic for the prompt induction of sleep in simple insomnia. When a single initial (bedtime) dose is effective for this purpose, the shorter action of the drug produces little or no hypnotic after-effect such as is occasionally observed with hypnotic doses of barbiturates; however, this possible advantage is likely to be lost in severe insomnia, when repeated doses of ethinamate are required to insure sleep throughout the night. For this reason, the drug is not primarily suited for use in patients requiring heavy or continuous sedation. The drug can be tried as a daytime sedative, however, for patients sensitive to barbiturates.

Ethinamate is readily absorbed by the gastrointestinal tract, and the major portion of the drug is rapidly destroyed in the body. About one-tenth to one-third of the oral dose is excreted in the urine. The liver is not the principal site of destruction of the drug in the body.

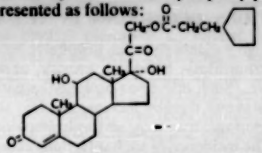
Ethinamate has not been found to produce toxic effects in man or experimental animals. Tachyphylaxis, tolerance, euphoria, and physical dependence have not been observed. The drug may be employed in the presence of impaired liver or kidney function, but until longer experience is gained, particularly with the prolonged use of the larger doses that may be required for effective hypnosis or continuous sedation, physicians should be alert for the occurrence of any unusual toxic effects.

Dosage.—Ethinamate is administered orally. The minimal effective hypnotic dose for adults is 0.5 gm. taken 20 minutes before retiring. Some patients may require as much as 2 gm. to induce sleep or a further dose on awakening before morning.

Preparations for use as stated for the foregoing drug are marketed under the following name: Valmid.

Eli Lilly & Company cooperated by furnishing scientific data to aid in the evaluation of ethinamate.

Hydrocortisone Cyclopentylpropionate.—17-Hydroxycorticosterone-21-cyclopentylpropionate.—The structural formula of hydrocortisone cyclopentylpropionate may be represented as follows:



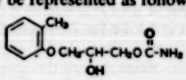
Actions and Uses.—Hydrocortisone cyclopentylpropionate, an ester of hydrocortisone, exhibits the same systemic actions and has the same potency as equivalent amounts of hydrocortisone. It is somewhat more palatable and more slowly absorbed from the gastrointestinal tract than the parent hormone. (See the monograph on hydrocortisone in New and Nonofficial Remedies.)

Dosage.—Hydrocortisone cyclopentylpropionate is administered orally. The dosage, expressed in terms of the parent drug, is the same as for hydrocortisone. (See the monograph on hydrocortisone in New and Nonofficial Remedies.)

Preparations for use as stated for the foregoing drug are marketed under the following name: Cortef Fluid.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of hydrocortisone cyclopentylpropionate.

Mephenesin Carbamate.—2-Hydroxy-3-*o*-tolyoxypropyl carbamate.—The structural formula of mephenesin carbamate may be represented as follows:



Actions and Uses.—Mephenesin carbamate, a salt of mephenesin, exhibits the same systemic actions and has the same uses as the parent drug. (See the monograph on mephenesin in New and Nonofficial Remedies.) Mephenesin carbamate is less soluble than mephenesin and therefore more slowly absorbed from the gastrointestinal tract. Although its duration of action is somewhat longer, the carbamate is not more potent than the parent drug in equivalent amounts.

Dosage. — Mephenesin carbamate is administered orally. The usual dose for adults is 1 to 3 gm. given three to five times a day, particularly after meals or with milk or fruit juice. Dosage for children should be reduced proportionately.

Preparations for use as stated for the foregoing drug are marketed under the following name: Tolseram.

E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of mephenesin carbamate.

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INFECTIONS OCCURRING IN THE HOSPITAL

Although patients go to the hospital to be cured, many acquire respiratory, intestinal, urinary, or wound infections there. Such infections prolong the patient's stay in the hospital and thereby increase the bed shortage, but, more important, they may seriously impair the patient's health. The incidence of such infections cannot be stated, because, unlike the weather, nobody talks about it. The development of antibiotic-resistant organisms, especially pyogenic micrococci, gives this subject increasing importance. Colebrook [1] in a recent survey found that outbreaks of puerperal septicemia still occur on maternity wards, outbreaks of gastroenteritis still occur in hospital nurseries and pediatric wards, wound infections following so-called clean operations are still seen, and cross infections still plague the medical wards.

The source of these infections often is not hard to find. Rogers [2] showed that in an infants ward the cribs, sheets, blankets, floor, floor polisher, bathtub, bedside table, nursing chair, thermometers, infant scales, towels, nurse's hands, and dirty linen basket—in fact practically everything—were contaminated with intestinal organisms of a specific type. He showed further that disturbing the bedclothes or towels caused a scattering of the same organisms in the air. Viable organisms of the same type were found in a sample of dust taken from a cubicle and kept undisturbed in a test tube for 27 days. Bedmaking scatters various pathogens through the air, especially pyogenic micrococci. Blankets are the worst offenders because they liberate relatively large quantities of lint and are rarely sterilized. Colebrook found hemolytic streptococci in freshly laundered hospital blankets. He also found that hospital eating utensils, bedpans, toys, and thermometers were inadequately sterilized after use. Changing the dressings of wounds was found to scatter various pathogens through the air, and dressings that are soaked through have been shown to permit pathogens from the air or other external contact to grow through to the wound surface rapidly.

1. Colebrook, L.: Infection Acquired in Hospital, Lancet **2**: 885-890 (Oct. 29) 1955.
2. Rogers, K. B.: The Spread of Infantile Gastro-Enteritis in a Cubicled Ward, J. Hyg. **49**: 140-151 (June-Sept.) 1951.
3. Rogers, K. B.: The Use of Cylinder Model Vacuum Cleaners, J. Hyg. **49**: 497-506 (Dec.) 1951.
4. Rountree, P. M.: Streptococcus Pyogenes Infection in a Hospital, Lancet **2**: 172-173 (July 23) 1955.
5. Lowbury, E. J. L.: Cross-Infection of Wounds with Antibiotic-Resistant Organisms, Brit. M. J. **1**: 985-990 (April 23) 1955.

From these observations it may be seen that the prevention of secondary infections in a hospital is an exceedingly difficult task. Although they cannot be entirely eliminated, much can be done to reduce their incidence. Dosing the patients with antibiotics provides no easy answer but rather aggravates the situation by facilitating the development of antibiotic-resistant organisms. The first line of defense is to block the channels of transmission of the pathogens, with antibiotics used only to treat those in whom other methods fail. The oiling of blankets and floors, which proved so effective during World War II, appears to have fallen into disuse. This should be revived. Colebrook states that autoclaving blankets under 5 lb. pressure for 20 minutes provides adequate sterilization and causes less shrinkage than ordinary laundering. Washing blankets in cetrimide (cetyltrimethylammonium bromide), although effective, has the disadvantages that it does not kill Pseudomonas aeruginosa and it may cause contact dermatitis in some patients. Rogers [3] showed that, although sweeping even an oiled floor causes bacterial contamination of the air, the use of a vacuum cleaner on an unoiled floor does not. A ventilating system in dressing rooms and operating rooms that introduces warm filtered air under positive pressure from ducts in or near the ceiling will carry particles toward the floor, whence they may be sucked out of the room by an exhaust fan at floor level. Such a system reduces wound contamination from the air to a minimum and entails no great expense. Unsterilized blankets, soiled dressings, and casts should be removed before the patient is wheeled into the operating or dressing room. In preparing a patient for operation the site of the incision should be thoroughly cleansed, working away from the site in ever-widening circles and never returning to the site, which should be covered as soon as it is prepared. Although these precautions are taught, they are often neglected, to the detriment of the patient. Open wounds should be dressed in a dressing room and not on a ward. Rountree [4] observed that, if a Streptococcus got into a wound with an antibiotic-resistant Micrococcus that was a potent penicillinase producer, parenterally given penicillin would not stop streptococcic infection.

Much good will result from a wider use of sterile rubber gloves, not only by physicians but also by nurses and technicians who come in contact with patients having any kind of infection. Such patients should be isolated in cubicles that can be sealed and fumigated if necessary and from which air is not circulated into the next cubicle or the corridor. Lowbury [5] says that cubicle isolation alone will not eliminate cross infections in pediatric wards, but, when it is combined with ultraviolet screens and special kitchens, it will be of help.

A great deal has been done to reduce the incidence of infections of all kinds, but the time has not yet arrived when we can let down our guard. In fact, there is some evidence that we should be increasingly on the alert to prevent infections from developing in patients after they enter the hospital. The indications are clear, but the necessary procedures require constant careful attention. Unless we give this attention, we will not be looking after the best interests of the patient or using our hospitals with maximal efficiency and infections acquired in the hospital will increase.

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FOOD POISONING

Food poisoning has been variously defined and in its broadest definition includes (1) illnesses due to preformed toxins that may cause acute gastrointestinal symptoms or acute disturbances of the central nervous system (these may be of bacterial origin or may be normal constituents of plants or animals, such as toadstools or various poisonous fishes eaten in the belief that they are foods); (2) food infections such as salmonellosis; (3) poisoning due to chemicals accidentally introduced into foods; and (4) food allergies. Such a definition has no practical value, and a strong feeling is developing that the term food poisoning should be abandoned in favor of specific etiological diagnoses. The fact remains, however, that, when several persons have sudden attacks of vomiting, abdominal pains, and diarrhea, until a specific diagnosis is made the clinician has only the term food poisoning to use as a working diagnosis. In 1951 food poisoning was a reportable disease in 30 states,[1] but, whether reporting an outbreak is required by law or not, it is to the advantage of the attending physician to report it in order that epidemiological and laboratory assistance may be obtained from the local health department. In a little over 50% of the reported cases, for various reasons an etiological diagnosis is never made.

Although micrococcic enterotoxins have been known to produce acute gastroenteritis since 1914, their importance as a major cause of outbreaks of food poisoning was not recognized until about 1930. Although most outbreaks of food poisoning occur outside the home and are traced to restaurants, caterers, church suppers, or food prepared for picnics several hours before eating, some do occur in the home and may be traced to a single bakery or other purveyor of prepared food for delivery. It was formerly believed that the commonest source of this type of food poisoning was an infected cut or whitlow on the hand of a food handler or an infected udder on a cow, but it is now evident that transfer of micrococci from the nose, with the organism entering food directly through dripping or sneezing or indirectly from the hands after blowing or otherwise touching the nose, is the usual mode of contaminating food, especially if the food handler has a cold. For this reason food poisoning may occur at any time of the year, but it is somewhat more prevalent in the winter than in the summer. Even if the food becomes heavily contaminated, no food poisoning will occur unless the organism is allowed to incubate for several hours at room temperature or higher. Unfortunately, placing the food in a refrigerator or cooking it in a large container will not inhibit the incubation of the organisms in the central portion for a matter of hours; cooking may actually increase this growth. For this reason flat containers not more than 4 in. deep are recommended, especially for storing food in a refrigerator.[2] Unfortunately, also, the enterotoxin is not destroyed by boiling for 10 minutes. Although it is destroyed by boiling for more than 15 minutes or heating at 150 F for 30 minutes or more, nutritionists discourage such practices because they destroy thermolabile vitamins.

Micrococcic food poisoning is most commonly traced to ham, chicken salad, the filling of pies and layer cakes, and various milk products, but almost any food may serve as a vehicle. Pasteurization does not prevent the development of Micrococcus pyogenes in products that are handled carelessly after pasteurization is complete. The incubation period of the attack is usually about 2½ hours but may be 30 minutes or 6 hours.[3] Although the attack may cause extreme prostration, recovery in one to five days is the rule, and the treatment is symptomatic. Control is made difficult by the facts that M. pyogenes is ubiquitous and is elaborated in a great variety of foodstuffs, breaks in sanitary techniques of handling food are common, and the public is rather apathetic toward tested means of prevention. Even heavily contaminated foods are not altered in taste, smell, or appearance. The clinical picture is so typical that the attending physician often lacks the incentive to prove the diagnosis, but this should be done so that information can be uncovered that will prevent future outbreaks. Specimens of food, vomitus, and feces should be collected promptly in sterile screw-topped containers and forwarded to the local health department. If this is delayed, the specimens on which a diagnosis could be based are often no longer available. In the laboratory, animal tests are generally unreliable. Toxigenic strains of M. pyogenes are coagulase-positive, but this means little in view of the fact that stools from 33% of persons with no gastrointestinal symptoms contain coagulase-positive micrococci that are probably harmless. Phage typing is now believed to be more important than serotyping in identifying toxigenic strains, and isolation of the same phage type from the feces or vomitus of a patient and from the suspected food is more conclusive than merely discovering a toxigenic phage type in either alone.

Salmonellosis is more properly considered a food infection than food poisoning, but until the diagnosis is made the investigation must proceed along the lines indicated for any type of food poisoning. Although the incubation period is usually about 12 hours, in some cases it may be only 6 hours, which would make it impossible to rule out enterotoxin poisoning without further investigation. Many of the cases of food poisoning of undetermined origin are due to Salmonella organisms, and about a third of all cases of salmonellosis in the United States are caused by Salmonella typhimurium. Where the incidence of salmonellosis is high there is always a high carrier rate in dogs and cats, although direct transmission from these pets is difficult to prove. The carrier rate in local food handlers in such areas is also high. Many sporadic cases are seen, in contrast to enterotoxin poisoning, which usually affects several persons. The usual vehicles include pork, turkey, custard, ice cream, and eggs. Duck eggs are especially likely to carry Salmonella organisms, and many outbreaks have been traced to egg powders, especially those with a rela-

1. Meyer, K. F.: Medical Progress: Food Poisoning, New England J. Med. **249**: 765-773 (Nov. 5) 1953; 804-812 (Nov. 12) 1953; 843-852 (Nov. 19) 1953.

2. Weiser, H. H.; Winter, A. R., and Lewis, M. N.: The Control of Bacteria in Chicken Salad, Food Res. **19**: 465-471 (Sept.-Oct.) 1954.

3. Warner, E. C.: Clinical Features of Food Poisoning, Practitioner **174**: 652-657 (June) 1955.

tively high moisture content. When cream puffs or custards are incriminated, the eggs are much more likely to be at fault than the milk, but in any case it is not wise to jump to conclusions as to what item of food eaten was to blame. Deaths from salmonellosis are rare except in very old or very young patients. Many other organisms may cause acute gastroenteritis, and Warner [1] believes that about 40% of those cases now reported as of unknown cause are due to a virus or what might be popularly called "intestinal flu."

Since sound preventive measures depend on a knowledge of the cause, the physician who first sees the patient is the key to the eradication of food poisoning. He should recognize his responsibility to promptly enlist the aid of the health department. The job of finding the cause is not easy, but teamwork will go far toward making food poisoning a rarity.

COMMISSION ON CHRONIC ILLNESS

The Commission on Chronic Illness, founded in 1949, will terminate its activities as an incorporated organization on June 16, 1956. Its founders (the American Hospital Association, the American Medical Association, the American Public Health Association, and the American Public Welfare Association) hoped that the commission would complete its work in five years or less, but it took just seven years, and now it believes that its functions can best be carried on by the founding organizations and other permanent agencies concerned with chronic illness. The 30 men and women now constituting the commission represent industry, agriculture, education, welfare, religion, journalism, law, labor, public health, medicine, hospitals, government, and the public. In addition, the commission members and staff have enjoyed the services of 41 expert technical advisers. The commission will meet for the last time in New York in February.

Among the major projects undertaken by the commission have been a study of the prevalence of chronic illness and needs for care of the chronically ill in an urban and a rural area, a study of the characteristics of patients requiring long-term care in institutions, and a study of 12 organized home care programs. One of its most valued contributions was the publication of the Chronic Illness News Letter. The commission has also maintained an active clearing house for information on chronic illness, but staff time and available funds did not permit the development and operation of this function to the extent warranted by the need and the demand.

Although the commission will complete its task in June, the sponsoring agencies will carry on individually to see to it that this group's excellent work is neither shelved nor lost. On February 1 the Council on Medical Service of the American Medical Association will assume responsibility for the continued publication of the Chronic Illness News Letter. This publication has done much to alter the attitude of the public toward the chronically ill. A real beginning has been made in this direction, and every effort will be made to carry on where the commission left off. There will be no change in policy or general format, and the editorial advisory committee will include Henry Mulholland, M.D., Edward L. Bortz, M.D., Dean Roberts, M.D., and Mrs. Lucille Smith. The commission is to be congratulated on its accomplishments, and it is heartening to know that, although the commission is officially to be disbanded, its work will continue without interruption.

THE FAITH HEALER

The medical profession recognizes the power of faith on the individual mind as a factor that may affect the condition of sick people. It also recognizes the fact that "faith healing," as such, has no accepted merit whereby it can be regarded as having remedial or curative effect in persons who are actually victims of organic disease.

It is true that persons have had what they believe to be relief or even cure of ailments that must be regarded as self-limited or imaginary, for the most part. There are even occasional instances in which diseases generally regarded as uniformly fatal reverse themselves without any explainable medical phenomena, whether or not the patient has had the ministrations of "Scientists" or other so-called healers. It should be realized, of course, that if such a phenomenon were to occur to an individual under "treatment" by one of these healers, the likelihood is that he or she would take the credit.

There have been reported in the medical literature evaluations of "faith healing," and the medical attitude is that such healing is perhaps a part of religious tradition, particularly in the United States, where there has been a wide variety of religious cults whose leaders claimed special healing abilities. These reports refer particularly to those individuals, frequently itinerants, who exhort, pray, and practice "laying on of hands." They have also been designated as "divine healers." [1] These persons are able to interest others, and may, in cases where no organic disease exists, influence the thinking of many lay individuals to such an extent that they believe they have had curative ministrations.

From a public health standpoint, it is known that such faith healers often display a woeful ignorance of public health measures. Diseased persons mingle in crowds in tents and other public meeting places and may very easily upset careful scientific efforts to suppress the spread of contagion or infection by accepted public health measures. The further danger exists that persons whose physical condition demands prompt and adequate scientific medical attention may, by delay or abandonment of such care, contribute to their needless early death.

Occasionally a "faith healer," without regard for fact, will publicize what he alleges to be medical acceptance of him and his teachings. In that, however, he is no different from the health cultists or the "patent medicine" manufacturers, who dearly love to play up "medical acceptance" as part of their stock in trade. It is realized, also, that the activities of some "successful" faith healers usually bring them ample monetary rewards. To this end, a good many of them carry "shills" as part of their entourage, who "throw away their crutches" at each performance.

1. Paulsen, A. E.: Religious Healing, J. A. M. A. 86:1519-1524 (May 15) 1926.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Recently, some of us were discussing the names of various individuals for service on some important committees of the American Medical Association. We were trying to find some younger men who seemed to be showing an interest in organized medicine so they could be trained to fill the shoes of those of us who eventually will pass along. During our conversations one man in the group remarked that he could not understand the attitude today of many of the younger men in medicine. His criticism was that too many of them seemed to be interested only in their own welfare. He told of a friend of his who had two younger associates, men between 35 and 40 years of age, who had been with the older man for several years. Neither of these younger men attended the meetings of their county medical society, although they were members in good standing. When they were approached by their elder associate about becoming interested in organizational affairs, they pleaded that they were entirely too busy. Why? Well, closer questioning brought out the fact that they were very much in debt. Both of them drove rather high-priced cars and were buying them on time. Both of them owned new homes, which also were mortgaged to the hilt. Their argument was that if they had any spare time they needed it to do things to keep up their properties. Both of them belonged to the country club and played golf three or four times a week. This was necessary, in their opinion, to keep acquainted with the best people so that they would be known as prosperous and successful physicians. Both of these young men were trying to establish themselves, pay off their debts, and finally be independent, but neither was looking into the future. Otherwise both would be concerned with what will happen to the private practice of medicine if new leaders in medicine are not now being trained in the problems peculiar to doctors. Neither seemed to care so long as their present incomes were satisfactory and they could live as well as "the chief," a man who spent many years to attain his present position.

Of course county medical society work often seems unimportant and inconsequential, even to the devoted followers of organized medicine. Thus the young uninitiated doctor cannot always understand why his older colleague is interested in and gives so much time to county society affairs. Nor can he understand why his colleague also is active in both state medical society and A. M. A. affairs. What, the young man asks, does his older colleague get out of his many hours of service to medicine? It is hard to explain at times what this man and countless others throughout the country are doing and why. If the younger man cannot appreciate that someone must do organizational work and that someday he should do the same to repay his debt to medicine, he is indeed unfortunate—and he really does not understand the Oath of Hippocrates, medical ethics, and the love of fellow man. When one devotes his life to service he cannot remain aloof of some parts of it; he must practice all phases of it. Thus many, many doctors give time and money and take criticism and abuse and come back for more because these are the men who are dedicated to principles. They try to be good doctors and good citizens; and when they do things others do not like, who are the first to complain? Those who never go to medical meetings. These latter are the same people who complain that the county society is run by a clique, that the leaders of their county society have "ganged up" to put over something, and they say the same thing about their state society. Then, if they go to the national medical meeting, they attend only the scientific sessions in which they are interested but never go near a meeting of the House of Delegates. However, since they learn that "the boys" who "run" the county and state societies are helping to run the great organization called the A. M. A., they say, "I told you so. Even the A. M. A. is run by a clique." Especially loud are the wails if the A. M. A. comes out with a policy they oppose. They forget they really know nothing about why the policy was adopted and ignore the fact that they did not attend meetings of the House and of its reference committees, meetings open to any member. Any report adopted by the House has first been studied by some committee.

Just one proof of the point I am trying to make is the mail I, as your president, have received concerning the A. M. A. action on social security. I have literally had hundreds of letters condemning the A. M. A. for opposing the voluntary coverage of physicians by social security. How strange this seems when it is a fact that the A. M. A. does not oppose social security for physicians if it is on a voluntary basis. Our House of Delegates several times has stated unanimously its position, which is against compulsory coverage by social security. It has advised the Department of Health, Education, and Welfare often that we are not against voluntary physician participation. Yet, despite publicity given the A. M. A. position, many physicians seem unaware of this.

May I plead with you younger men to take an active part in your county society. If you do not like what your elected officers do, throw them out and elect others. If you want to continue to practice medicine independently, become active in your local county society. You can have what you want but must work for it and earn it by service. You owe your forebears in medicine a debt you can never pay. Do more than complain—join up and work.

ELMER HESS, M.D., Erie, Pa.

ORGANIZATION SECTION

The December bulletin of the Joint Commission on Accreditation of Hospitals (660 N. Rush St., Chicago; Kenneth B. Babcock, M.D., director) is being reproduced for the information it contains that will be of interest to many physicians.

MEDICAL RECORDS

Medical records are an important tool in the practice of medicine. They serve as a basis for planning patient care, they provide a means of communication between the physician and other professional groups contributing to the patient's care, they furnish documentary evidence of the course of the patient's illness and treatment, and they serve as a basis for review, study, and evaluation of the medical care rendered to the patient. For these reasons the Joint Commission on Accreditation of Hospitals considers the quality of medical records an important indication of the quality of patient care given in a hospital.

Since medical records reflect patient care, the Commission evaluates a medical record on the basis of whether or not it contains sufficient recorded information to justify the diagnosis and warrant the treatment and end results. In agreement with this principle, the Commission has established certain standards of record keeping which it thinks are essential for good patient care.

I. *Content—Medical Records Should Contain the Following Information:*

1. Identification Data

2. Provisional Diagnosis

There should be a provisional or admitting diagnosis made on every patient at the time of admission. If a patient requires hospitalization, the hospital staff deserves this information to proceed intelligently.

3. Chief Complaint

4. Present Illness

5. History and Physical Examination

Only physicians and house staff are competent to write or dictate medical histories and physical examinations. All pertinent positive and negative findings should be recorded. Nurses, medical record librarians, or secretaries should not be permitted to take medical histories.

6. Consultations

Consultations imply an examination of the patient and the patient's record. The consultation note should be recorded and either signed or authenticated by the consultant.

7. Clinical Laboratory Reports

The original signed laboratory report should be entered in the patient's record. Duplicates are filed in the laboratory.

Reports from laboratories outside the hospital are acceptable in lieu of tests performed in the hospital if the following safeguards are maintained:

a. Work is done in a laboratory approved by the city or state. Laboratory work performed in a physician's office by a technician, nurse, or office assistant is not acceptable. Since the hospital is held responsible for the quality of laboratory work reported in the medical record, it must limit outside laboratory work to approved laboratories.

b. The test is recent enough to be pertinent to the individual case. For example, a serological test for syphilis or an Rh determination done any time during the prenatal period would be acceptable. A urinalysis done prior to 48 hours of admission would not.

c. The original laboratory report is made part of the medical record.

8. X-ray Reports

The original signed radiological report should be entered in the patient's record. Duplicates are filed in the department.

9. Tissue Report

Since all tissues removed in surgery are sent to the laboratory, at least an acknowledgment that the tissue has been received and a gross description should be made part of the record. If a microscopic examination is done, a description of the findings should be made a part of the record. Whether or not a microscopic examination is done should be determined by the medical staff and the pathologist according to the rules and regulations of the hospital.

10. Treatment—Medical and Surgical

All treatment procedures should be documented in the medical record. Except in cases of grave emergency, the patient should receive a complete diagnostic work-up before surgery. Operative notes should be dictated immediately after surgery and should contain both a description of the findings and a detailed account of the technique used and tissues removed.

11. Progress Notes

Progress notes are important in that they give a chronological picture and analysis of the clinical course of the patient. The frequency with which they are made is determined by the condition of the patient.

12. Final Diagnosis

A definitive final diagnosis based on the terms specified in the Standard Nomenclature of Diseases and Operations should be written.

13. Summary

A summary of the patient's condition on discharge and course in the hospital is valuable as a recapitulation of the patient's hospitalization.

14. Autopsy Findings

When an autopsy is performed a complete protocol of the findings should be made a part of the record.

II. *Signatures*

1. In hospitals without house officers the attending physician should separately sign the history, physical examination, operative report, progress notes, drug and other orders, and the summary. Standing orders should be reproduced on the record and signed by the physician.

2. In hospitals with house officers, the attending physician should countersign at least the history, physical examination and summary written by the house officer. Aside from the fact that this is a legal requirement in many states, it is a protection to the individual physician. It is not considered necessary to countersign progress notes or drug and treatment orders written by house officers. In all instances a physician should sign the clinical entries which he himself makes.

3. A single signature of the physician on the face sheet of the medical record does not suffice to authenticate the entire content of the record.

4. The use of rubber stamp signatures is acceptable under the following strict conditions:

a. The physician whose signature the rubber stamp represents is the only one who has possession of the stamp and is the only one who uses it.

b. The physician places in the administrative offices of the hospital a signed statement to the effect that he is the only one who has the stamp and is the only one who will use it.

5. Initials in place of a full signature are acceptable provided that the initials can be recognized as having been placed there by a particular physician who can be identified by those initials.

III. *Obstetric Records*

There should be a prenatal history and physical examination on every obstetrical patient. If the hospital and medical staff permit and records are of good quality on forms approved by the hospital, a copy of the prenatal record kept by the physician in his office may be substituted for a history and physical examination done in the hospital.

IV. *Readmissions*

If a patient is re-admitted within a month's time for the same condition, the previous history and physical examination with an interval note will suffice.

V. *Nurses' Notes*

The Commission has no requirements concerning nurses' notes. It is the responsibility of the local medical and nursing staffs to develop policies concerning the type and extent of nurses' notes to be kept.

VI. *Forms*

1. The Joint Commission on Accreditation of Hospitals recommends no specific medical record forms. Records are evaluated on the basis of content and whatever forms the hospital finds most useful are acceptable. It is common experience that check-off lists do not adequately provide sufficient information to substantiate the diagnosis and treatment.

2. Short Forms

A short form medical record is acceptable in certain treatment and diagnostic cases of a minor nature which require less than 48 hours' hospitalization. Short forms may be appropriate for such conditions as tonsillectomies, cystoscopies, lacerations, plaster casts, removal of superficial growths, and accident cases held for observation. The short form should at least include identification data, a description of the patient's condition, pertinent physical findings, an account of the treatment given and any other data necessary to justify the diagnosis and treatment. The record should be signed by the physician.

VII. *Filing and Maintenance of Medical Records*

1. Current records should be completed insofar as possible within 24-48 hours.

2. After discharge, records should be completed insofar as possible within 10-15 days.

3. A system of identification and filing to insure the rapid location of a patient's medical record should be maintained. The unit number system is suggested; however, a serial number system or modification of this is acceptable.

4. Records should be indexed according to disease, operation, and physician.

5. If medical records are coded, it is suggested that the Standard Nomenclature be used.

VIII. *Preservation of Medical Records*

The Joint Commission on Accreditation of Hospitals has no standards governing the preservation of medical records. The length of time a medical record is preserved is a matter which should be determined by the local hospital and local laws.

Methods of preservation by microfilming or other means of storage is a decision for the individual hospital to make.

IX. *Ownership*

The medical record is the property of the hospital and is maintained for the benefit of the patient, the physician and the hospital. It is the responsibility of the hospital to safeguard the information on the record against loss, tampering, or use by unauthorized persons.

CONFERENCE ON GRADUATE EDUCATION

As announced in THE JOURNAL, Jan. 14, the Council on Medical Education and Hospitals will co-sponsor this year with the Advisory Board for Medical Specialties a conference on graduate education during the Annual Congress on Medical Education and Licensure in Chicago, Feb. 11-14. The one-day conference will be held on Saturday, Feb. 11, and will consist of a series of papers on various aspects of residency training during the morning and a critique of these papers during the afternoon, with the morning speakers serving as panelists for the discussion. The fact that the Council and the Advisory Board are sponsoring a program of this type is a recognition of the increasing importance of this phase of medical education. The conference is somewhat experimental in nature, being the first that the two organizations have planned. The speakers and discussants are all men eminent in their particular fields. The subjects they are presenting will have practical application for physicians responsible in one capacity or other for the conduct of residency programs in their own hospitals.

The Council and the Advisory Board are to be commended for recognizing the need for a meeting of this type and for providing a forum where representatives from hospitals throughout the country, those affiliated with medical schools and those not so connected, can meet to discuss mutual problems. In view of the already heavy advance registration, it can be anticipated that the conference will be a productive one and one that will likely set a precedent for future annual conferences of this type.

REPRINT ON ESTIMATING LOSS OF VISION

The Council on Industrial Health, American Medical Association, 535 N. Dearborn St., Chicago 10, announces the availability of the following reprint: "Estimation of Loss of Visual Efficiency," published in the *A. M. A. Archives of Industrial Health*, October, 1955. The article details several important changes in methods of appraising vision losses due to accident or disease and includes a glossary of the technical terminology. Single copies will be furnished without charge by the Council on Industrial Health. Prices on quantity orders are available through the Order Department of the American Medical Association.

CALLING ALL NURSES

The national *Today's Health* Committee of the Woman's Auxiliary has launched a special subscription campaign for registered nurses, featuring a two-dollar rate during the months of January, February, and March. Local committee members will contact all nurses in their areas by telephone or in person. The Future Nurses Association, made up of high school girls interested in nursing, also will cooperate in the project. Several auxiliaries

already have planned special luncheons and teas to acquaint nurses in hospitals and clinics with *Today's Health* magazine.

REGIONAL STANDARD NOMENCLATURE INSTITUTES

To provide persons in various parts of the country an opportunity to "brush up" on the use of the Standard Nomenclature of Diseases and Operations, the American Medical Association has scheduled its first regional Standard Nomenclature institute Feb. 6-8 at the Hotel Dennis, Atlantic City, N. J. The three-day short course will offer instruction on the best ways of utilizing the Nomenclature in the hospital, doctor's office, or clinic. Lectures on theory will be given by Adaline C. Hayden, C.R.L., associate editor of Nomenclature, and on anatomy by Edward T. Thompson, M.D., chief of programs operations, Division of Hospital Facilities, United States Public Health Service, Washington, D. C.

Registration, limited to the first 100 applicants, is not restricted to registered medical record librarians. Anyone who is planning to install the system or is already using it and who is employed as clinic clerk, doctor's secretary or receptionist, nurse, or physician may attend. Tuition is free. Applications should be sent to Mrs. Hayden at A. M. A. headquarters in Chicago. Another institute will be held at A. M. A. headquarters in the fall.

A. M. A. ANNOUNCES 1956 RADIO PLANS

The American Medical Association's new radio transcription series will be enlivened by music during 1956, the Bureau of Health Education has announced. The Bureau plans to releaese three new series of 13 programs each for use by medical societies over local radio stations. The first will feature a "music with your meals" theme, with an instrumental trio rendering folk songs, ballads, and semiclassics. Dr. W. W. Bauer, Bureau Director, will give the medical commentary based on 13 different phases of diet and nutrition. The second series, also on a musical theme, will be entitled "Summer Serenade" and will deal with summer situations such as having fun while avoiding illness and accidents. This series is intended as a replacement for previous series dealing with summer health topics. The format and subject matter for the third series have not been selected as yet, although it will be either musical or dramatic in character. Probable release dates for the new program will be April 1, Aug. 1, and Nov. 1.

NEW BOOKLETS FOR MEDICAL SOCIETIES

Two booklets of vital interest to medical societies will be published by the American Medical Association early in February. The first, "Guides for Medical Society Grievance Committees," reviews the findings and recommendations of the special committee on grievance committees appointed by the Board of Trustees. The second publication, "Report of the Survey on County Medical Society Activities," will include data on society meetings, budgets, educational and scientific programs, personnel, building facilities, the work of various kinds of committees, and the extent of public relations activities. Copies of both booklets will be mailed to each state and county medical society. Additional copies will be available on request from the Council on Medical Service.

COUNCIL ON MEDICAL SERVICE

A STUDY OF MATERNAL MORTALITY COMMITTEES

This is part 2 of a series of articles by the Committee on Maternal and Child Care of the Council on Medical Service reviewing the organization and operation of maternal mortality study committees. The purpose of this specific study is to obtain information that may be utilized in the preparation of guides for developing and operating maternal mortality committees in other areas in the United States. The material to follow is concerned with the Maternal Mortality Study Committee of the Columbus (Ohio) Obstetric-Gynecologic Society (recently made an official committee of the Columbus Academy of Medicine).

FRANKLIN COUNTY MATERNAL MORTALITY STUDY

History.—The Franklin County Maternal Mortality Study is conducted by the Maternal Mortality Study Committee of the Columbus (Ohio) Obstetric-Gynecologic Society. The society and committee members finance the work, and the project has the approval of the Columbus Academy of Medicine. Operation began in 1948 with two physicians interested in the scientific and professional problems associated with the community's maternal mortality rate. The program developed rapidly under their direction, and, at the end of the first year, the Columbus Obstetric-Gynecologic Society voted to sponsor the project as an official function of the society.

Some of the purposes for promoting the study were: (1) to assure adequacy of maternal care; (2) to offer an educational (training) program (including early diagnosis of complications, and prompt, adequate consultation) for the medical profession, allied personnel, and the lay public (especially newlyweds and expectant mothers); and (3) to introduce and maintain standards of classification and nomenclature (recommended by the World Health Organization and American Committee on Maternal Welfare) so that the Franklin County Maternal Mortality Study results could be compared with the results and statistics of similar studies. The immedi-

Committee members are W. L. Crawford, M.D., chairman, Rockford, Ill.; R. B. Chrisman Jr., M.D., Coral Gables, Fla.; Philip S. Barba, M.D., Philadelphia; Harold S. Morgan, M.D., Lincoln, Neb.; J. L. Reichert, M.D., Chicago; Garland D. Murphy, M.D., El Dorado, Ark.; Howard A. Nelson, M.D., Greenwood, Miss.; and Donald A. Dukelow, M.D., consultant, Chicago.

ate objective was to present to the community a project to be developed and maintained by physicians for the benefit of mothers, expectant mothers, and unborn children.

The committee now has three committee members (including the two original members) and two alternate assistants, all of whom belong to the local obstetric-gynecologic society. These members are appointed (reappointed if willing to continue to serve) annually by the president of the obstetric-gynecologic society. The committee work is divided between the members by means of a rather flexible, voluntary method. The chairman of the committee is chosen by rotation among the committee members each year, and cases are investigated by whichever member is the least busy at the time a case is reported. In any event, all cases are usually studied within one month after notification.

The Ohio State Medical Association has recently formed a Committee on Maternal Health consisting of one representative from each of the 11 counselor districts and has asked each county medical society to form a local committee to assist the state association study. In view of this development the local committee, which has conducted the maternal mortality study in Franklin County for the past eight years, has been appointed the official committee of the Columbus Academy of Medicine.

Scope of Study.—A maternal case to be studied by the committee is defined as one in which a woman dies in Franklin County (resident or nonresident) who is in a state of pregnancy or within 365 days following the date of termination of her pregnancy, regardless of the length of gestation and including those cases of alleged criminal abortions. The term maternal death is applied to include all deaths in women, with either a nonviable or viable fetus, dying during pregnancy, labor, or the puerperium from causes directly due to the pregnant state, such as abortion, ectopic pregnancy, or placenta praevia, as well as associated causes such as heart disease, embolism, tuberculosis, and other accidental complications of pregnancy, but not necessarily limited to these alone. It is well to note that associated causes, such as heart disease, must have been aggravated by pregnancy in order to be classified as a maternal death. If it is fairly well established that the patient would have died from the disease regardless of whether she became pregnant or not, it is classified a nonmaternal death. (An "obstetric death" is considered a "maternal death.")

This committee does not yet study maternal morbidity cases; no neonatal and fetal deaths are referred to it. However, its work has inspired the formation of a perinatal mortality committee of the Central Ohio Pediatric Association, which is now in its formative stage and is developing a pilot study. At the present time, in conjunction with the perinatal mortality committee, the maternal mortality committee is planning to study the correlation between mortality of the mother and what happens to the newborn infant.

Operation: Agencies and Personnel Involved.—The attending physician fills out the official death certificate, which the undertaker must file with the health department. The vital statistics unit of the health department checks to see if the certificate fits the definition of a maternal case; if so, the assistant registrar notifies the chairman of the Maternal Mortality Study Committee. If the death certificate does not mention pregnancy but indicates that the woman is of childbearing age (which is taken as between the ages of 15 to 45 years), the vital statistics office checks the last name of the death certificate with the last name of all birth certificates of the same name that have been filed within the last 365 days. By this method maternal cases are occasionally found in which gestation was not indicated on the death certificate. In addition, a few maternal cases are picked up through indirect methods. One case was reported by a neighbor; the state of pregnancy had not been indicated on the death certificate. Another case had been reported to the committee by a pathologist; this case had been a criminal abortion, yet the state of pregnancy (as in the previous case) had not been indicated on the death certificate.

The committee has a regular maternal mortality study questionnaire to aid in gathering data. This questionnaire is a modification of the one used by the New York Academy of Medicine, the Philadelphia County Medical Society, and the Children's Bureau for their "Fifteen State Study." Recently it has been revised to meet certain changes in terminology and coding used in the Sixth Revision of the International Classification of Disease, Injuries, and Causes of Death and to serve demands of several years of the study. Copies of the questionnaire are supplied to hospitals and physicians so that, when a maternal case does appear, the physician can fill out the questionnaire promptly and forward it to the committee. Most physicians have been cooperative in this respect. Personal interviews are used to get detailed information on prenatal care, where hospital records are not complete or when incomplete questionnaires are received from doctors. Hospital records are reviewed by a committee member in all cases. The committee is alert for the appearance of a maternal case and in many instances may not have to wait for health department notification; in fact the physician concerned may, himself, notify the chairman by phone. No waiting period between notification and investigation is observed, nor has such a waiting period ever been thought necessary.

Only one difficulty of any importance has been encountered in the study. The particular maternal case involved a homicide situation. When approached by the committee in its efforts to secure information from the hospital records, the hospital administrator was reluctant to make the records available to the committee. Therefore, the committee appealed to the members of the hos-

pital medical staff. When it was made plain that the purpose of the study was that of a purely scientific endeavor, the staff voted unanimously to make available to the committee all records pertaining to the care of the woman.

In the processing of data, the committee members secure their reference information through the completed questionnaire. This material is abstracted and presented at an annual meeting of the Columbus Obstetric-Gynecologic Society. Abstracts of all cases for that particular year are combined in a booklet. A typical abstract consists of eight items: (1) age, (2) date of delivery, (3) date of death, (4) history, (5) antepartum, (6) intrapartum, (7) postpartum, and (8) cause of death. Item (1) also includes race, occupation, para, gravida, cesareans, and abortus. Item (2) also includes type of delivery, whether or not the infant is term, and whether or not the infant is hospital-delivered. Item (5) would include all prenatal care and developments occurring at that time. All other items are self-descriptive.

Data are kept confidential by use of a two-sheet questionnaire. The first sheet identifying the mother, the physician, the child, and the type of delivery is detached from the second after both are given the same serial number, registration number, and code number. The second sheet then appears only as a scientific study of a specific case involving no known persons. All reporting pertaining to the case is kept anonymous and at no time does the committee divulge the identity of any patient, physician, or hospital concerned with handling the case.

The Maternal Mortality Study Committee meets in the homes of the committee members at such intervals as are deemed necessary (approximately 12 times a year) to study the collected data and prepare them for presentation at a later date. These meetings are closed to all physicians except those who are members of the committee. The committee meets each spring with the Columbus Obstetric-Gynecologic Society to present the cases as noted previously. At this annual meeting, all the society's members may attend. Associate society members, who are obstetric and gynecology residents in the various hospitals, may also attend. All physicians who have maternal cases to be presented are specifically invited, as are the anesthesiologists involved and the consultants having knowledge of a particular case. All members of the academy of medicine are invited to attend these annual meetings also. The health commissioner of the Columbus Health Department and the registrar of vital statistics (a physician) of the Columbus Health Department are both honorary members of the society and as such are privileged to attend the society's meetings. The coroner and assistants who are all physicians have standing invitations. The booklet summarizing the cases is distributed to all in attendance and the chairman of the Maternal Mortality Committee presents all cases. After a case has been presented, the attending physician may identify it as being his own and discuss the case if he wishes; this is the procedure in most cases. Other physicians who have knowledge of the case may contribute their interpretations of the problems involved. In each case the pathological report has been included in the abstract; the pathologist does not present his findings personally to the group unless he chooses to do so.

The criteria used in determining whether death was maternal or nonmaternal are based upon the definition of a maternal death (as previously given) and the clinical judgment of the society members. Some committee and society members have expressed the opinion that further study is desirable to set up more uniform criteria. After careful evaluation, the death is classified as preventable or nonpreventable according to a majority vote by the members present. Responsibility for preventable deaths is ascribed to the patient or to personnel. Patient responsibility rests upon her cooperation in the prenatal care given to her—she must submit to all necessary physical and laboratory examinations, follow the therapy that is prescribed, and take the necessary medicines. Personnel responsibility includes attending or consulting physician, resident, intern, nurse, or other hospital personnel administering to the needs of the patient. The physician's responsibility rests with his judgment, recognition of complications, use of consultation, and use of therapy appropriate to the disease.

Follow-Up and Disposition of Cases.—Written reports of the findings at the annual committee-society meetings are not sent to the persons involved. The attending physician (and residents and interns) interested in a particular case may not know the opinion of the society concerning that maternal death unless he attends the meeting or reads the report published annually, and, although this report does not state whether a death was or was not preventable, it is readily apparent to the reader. The committee keeps on record the maternal mortality study questionnaires and the booklets containing the abstracts with the society's written opinions classifying the death as maternal or nonmaternal, preventable or nonpreventable, and patient or personnel responsible. No records are kept of deliberations leading to a vote on a maternal case. The Maternal Mortality Committee has published two articles in the lay press. The first article, on the front page of the newspaper, was entitled "Women Needn't Die in Child Birth" and was published initially to stimulate lay interest in, and appreciation for, the improvement that had occurred in maternal care in Columbus and the resultant lower maternal mortality rate. In an effort to arouse statewide physician interest, a preliminary summary of the maternal mortality study for the first four-year period was published in *Ohio's Health* in June, 1952, and the five-year survey appeared in the *Ohio State Medical Journal* in May, 1955. Members of the Columbus Academy of Medicine are apprised of the maternal mortality study during the year through the pages of the Academy *Bulletin*, which is the monthly publication of the local county medical society and is, therefore, the principal medium for the transmission of the study's facts and features to the 700 physi-

cians of Franklin County. The committee prepared an interesting exhibit depicting the major maternal killers for the American Medical Association meeting in Atlantic City of this year (1955) and the annual meeting of the American Academy of Obstetrics and Gynecology in Chicago (1955). The exhibit had been previously demonstrated at the Ohio State Medical Association annual meeting (1954). The teaching hospitals utilize the findings of the study in their educational program for medical students and interns.

Results: Statistical Analysis.—The first year, 1948, of the Franklin County Maternal Mortality Study revealed a mortality rate of 1.67 per 1,000 live births. This included all maternal deaths occurring in Franklin County (including Columbus) regardless of residency. The fifth year of the study, 1952, showed a rate of 0.68 per 1,000 live births, and in the seventh year, 1954, the rate was 0.41 (based on 16,964 live births recorded in 1954). This latest and lowest rate represents seven maternal deaths so classified from a total of 21 maternal cases carefully evaluated in the study. Of these seven maternal deaths, two were due to hemorrhage, two to infection (no puerperal fever), and one each from amniotic fluid infusion, ruptured cerebral aneurism, and subarachnoid hemorrhage. No deaths resulted from toxemia or abortion in Franklin County in 1954.

In the first five years of the study, from 1948 through 1952, of the 82 maternal cases studied, 61 were classified as maternal (obstetric) deaths and 21 as nonmaternal deaths. Diseases associated with nonmaternal deaths included hepatitis, cerebral vascular accident, ileitis, chronic pulmonary diseases, colitis, burns, carcinoma, sarcoma, acute abdomens, heart disease, poliomyelitis, as well as categories such as alleged homicides, accidents, and surgical procedures. Among the 61 (100%) maternal deaths, 38 (62.3%) were classified as preventable, responsibility of personnel, and 10 (16.4%) were classified as preventable, responsibility of the patient; 13 (21.3%) were classified as nonpreventable. The table shows maternal deaths by primary cause of death in Franklin County, Ohio, from 1948 through 1952.

Conclusions.—During the first seven years of study, 1948 through 1954, the annual maternal mortality rate (including all maternal deaths occurring in the county) for Franklin County declined from 1.67 to 0.41 per 1,000 live births. Although statistical significance of rates based on these relatively few maternal deaths is questionable, nevertheless, the trend of desired results is apparent. The committee members and physicians of Columbus believe that the maternal mortality study program has been worthwhile. A state study of maternal deaths has been started by the Ohio State Medical Association. The Columbus pediatricians and obstetricians have established a perinatal mortality study that is being co-sponsored by the Central Ohio Pediatric Association and the Columbus Obstetric-Gynecologic Society. The local anesthesiologists are considering the establishment of an anesthesia mortality study committee, and a pelvic cancer delay committee has been established under the sponsorship of the Columbus Obstetric-Gynecologic Society.

The Maternal Mortality Study Committee recommends continuing efforts in the study of maternal deaths and believes that minimal standards for obstetric care should be adopted as an aid to hospitals and for the benefit of future mortality studies. The committee is developing a set of minimal obstetric standards, which aim to eliminate needless deaths. These will be published in the near future. The decision as to where to draw the line concerning minimal standards is difficult because it is apparent that a patient can receive minimal care and still die. Merely because a patient received minimal care does not mean that all was done for the patient that should have been done. It is undesirable to present an excuse crutch for those who seek one. Furthermore, it is realized that many normal patients do quite well who do not receive minimal care, and it might be thought that in those cases minimum standards were of less value. Nevertheless, the committee does feel that such standards do have distinct value as an educational guide, and, if each standard is met, no patient may die a "preventable death."

Primary Cause of Maternal Deaths for Five-Year Period, 1948-1952 *

Cause of Death	No.	%
Hemorrhage	12	19.7
Infection	14	22.9
Toxemia	12	19.7
Cardiac	8	13.1
Embolism	5	8.2
Anesthesia	2	3.3
Hyperemesis	2	3.3
All others †	6	9.9
Total	61	100.0

* Melling, R. L. and Ruppersberg, A., Jr.: Maternal Mortality in Franklin County: A Five-Year Study, Ohio M. J. 50: 445 (May) 1954.
† Diabetes, pneumonia, intestinal obstruction, nephronephrosis, tetany, and anemia.

The study committee has encountered only one adverse situation to its study and that involved a case of homicide with the obvious legal entanglements surrounding such situations. The committee has never had legal difficulties. Since its inception, legal advice indicated that as the committee is engaged in a purely scientific study that is not used for disciplinary or punitive purposes, its material could not properly be submitted as evidence in court. It is apparent that it would be very difficult for scientists to pursue scientific studies if the information uncovered, in order to improve a scientific pursuit, was subject to submission into court and used to discipline or punish the scientist's colleagues. The laws and courts of Ohio recognize that scientific studies are necessary for progress, and, therefore, no impediment is placed in their path. The community recognizes this project on the part of the physicians as one in which there is no personal gain for the physicians but all benefits accrue to the mothers, expectant mothers, and unborn children.

MEDICAL NEWS

ALABAMA

Narcotic Violation.—Dr. Emerson Ward Blakney, Reform, pleaded guilty in the U. S. District Court at Birmingham to a violation of the federal narcotic law. On May 12, 1955, sentence was suspended, and he was placed on probation for three years.

Personal.—Dr. Louis L. Friedman, Birmingham, has been appointed coordinator of the poliomyelitis vaccine program for the state of Alabama.——Dr. Wyatt Heflin, Birmingham, recently celebrated his 95th birthday. Among the gifts received by Dr. Heflin was a large bouquet from the alumni of Jefferson Medical College of Philadelphia, of which he is the oldest living alumnus.——Dr. Charles Alston Thigpen, Montgomery, recently celebrated his 90th birthday.

Meetings on Mental Health.—The Lee County Mental Health Association has issued a brochure outlining its purposes, activities, and schedule of open meetings for the year. Dr. Frank A. Kay, Birmingham, will discuss "Mental Illness in the Community" in Thach Hall Auditorium at 7:30 p. m., Feb. 6. "Breakdown," a mental health film, is scheduled for March 5 in the auditorium. Scheduled for the same hour and place on April 2 is a talk by Mrs. Edwina Mitchell, superintendent, Julia Tutwilder Prison, "Prisons—A Challenge to Mental Health Workers." The annual meeting of the association, May 6, will include a demonstration of how a mental health clinic team works.

ARIZONA

Personal.—Dr. John B. Alsever, formerly instructor in pathology at Syracuse (N. Y.) University College of Medicine, has been appointed the first full-time medical director of Southwest Blood Banks, Inc., with headquarters in Phoenix.

Indian Health Survey.—The University of Arizona bureau of ethnic research recently received a grant from the U. S. Public Health Service for a survey that will cover the social and economic resources available for Indian health purposes in Arizona, New Mexico, Nevada, Utah, and Colorado.

Narcotic Violation.—Dr. Waldo J. Lehman, Chino Valley, pleaded guilty to violation of the federal narcotic law in the U. S. District Court at Phoenix and on Aug. 19 was sentenced to serve a term of three years and placed on probation for two years, said probation to commence on the completion of the sentence of three years.

Memorial to Doctors Holmes.—The board of trustees of the Phoenix YMCA recently announced that the round-up banquet and meeting hall of the YMCA building, unfinished since the structure was occupied three years ago, will be completed as a memorial to Drs. Fred G. and Fred W. Holmes, who were drowned on a fishing trip Aug. 7, 1955.

Auxiliary Dinner.—The Tucson Medical Center auxiliary recently gave a donor dinner, at which Dr. Arthur J. Present delivered an address. Among those contributing to the entertainment features were Drs. Sherwood P. Burr, Tucson, who played the banjo; Harriet S. Baritell, Clarence L. Robbins, and Elmer E. Yeoman, Tucson, who presented a comedy pantomime of "Enoch Arden"; and Frank A. Shallenberger Jr., Tucson, a "gravel-voiced medicine man."

CALIFORNIA

Fellowship in Cancer Chemotherapy.—This fellowship is available on the tumor chemotherapy service, department of medicine, Stanford University School of Medicine, San Francisco, for the year July 1, 1956, to June 30, 1957. It pays a monthly stipend of $300, provides an opportunity for clinical investigation and basic research in the field of tumor chemotherapy as well as for training in basic and clinical hematology. The appointment is for one year but may be renewed for an additional year. Anyone interested should communicate with Dr. Byron E. Hall, Tumor Chemotherapy Service, Department of Medicine, Stanford University School of Medicine, San Francisco.

Courses in Electrocardiography and Radioactive Isotopes.—A course designed primarily for the physician who desires basic background in the interpretation of electrocardiograms will be offered by the University of Southern California School of Medicine, medical extension division, Los Angeles, Feb. 10-12, at the Hotel Statler in Los Angeles (tuition, $50). There will be opportunity for the physicians to interpret electrocardiograms under supervision of the university faculty.——The University of Southern California School of Medicine, medical extension division, Los Angeles, will hold sessions on Friday afternoons, 4-5 p. m., from Feb. 10 to June 22. The course is part of a three-part program offered to afford training to physicians who wish to apply for certification by the Atomic Energy Commission as well as to physicians who merely desire to know more about the possibilities of radioactive isotopes. For information write: Dr. Phil R. Manning, Director Medical Extension Education, U. S. C. School of Medicine, 2025 Zonal Ave., Los Angeles 33.

COLORADO

Society News.—Newly elected officers of the Colorado Radiological Society include: Dr. Raymond R. Lanier, Denver, president; Dr. James W. Lewis, Colorado Springs, vice-president; Dr. Lorenz R. Wurtzebach, Denver, treasurer; and Dr. Dorr H. Burns, Denver, secretary.

Hospital News.—An anonymous donor has supplied $350,000 of the $750,000 campaign goal of the National Jewish Hospital, a free, nonsectarian hospital in Denver. The hospital plans a building project that will include a three-story rehabilitation center and auditorium and will allow for a 35% increase in adult population.

CONNECTICUT

Personal.—Dr. Joseph L. Melnick, professor of epidemiology, Yale University School of Medicine, New Haven, has gone to India under the auspices of the Rockefeller Foundation to participate in research on virus diseases. He will be working at the virus research center recently established by the Indian Council on Medical Research and the Rockefeller Foundation in Poona, in Bombay Province.

University News.—Dr. Robert H. Parry of Cefniwrch, Cricoieth, North Wales, has been appointed visiting professor in public health at the Yale University School of Medicine, New Haven. ——Dr. Walter Herrmann, who has been appointed instructor in obstetrics and gynecology, received his M.D. degree at the University of Geneva, Switzerland. He has served on the resident staff at the Yale-New Haven Medical Center and also as an American Cancer Society fellow at Yale.

Hartford Society Spring Lectures.—The Hartford Medical Society will present the following lectures at the Hunt Memorial, 38 Prospect St., Hartford, at 8:30 p. m.:

Feb. 6, Surgical Treatment of Coronary Insufficiency, Claude S. Beck, Cleveland.
Feb. 20, Surgical Aspects of Upper G-I Bleeding, Ralph Colp, New York.
March 5, Modern Techniques in X-Ray Diagnosis, Benjamin Felson, Cincinnati.
March 19, Current Concepts of Heart Failure, Eugene A. Stead Jr., Durham, N. C.
April 2, Medical Aspects of Bone Disease, Isidore Snapper, New York.
April 16, Ulcerative Colitis, Albert F. R. Andressen, Brooklyn.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Emergency Medical Plan.—A new 24-hour emergency medical call plan was recently inaugurated for the communities of Ansonia, Derby, Seymour, Shelton, and Oxford under the sponsorship of the Medical Society of the Lower Naugatuck Valley. A central switchboard in Ansonia receives all emergency calls. The operator then contacts one of the 26 physicians listed on the emergency roster who may be nearest to the scene of the emergency. The plan, which operates seven days a week and is available without toll charges to more than 52,000 residents in the five communities, is the 17th community emergency call system to be sponsored by medical associations in Connecticut. Plans are operating in other communities as follows: Bridgeport, Danbury, Greenwich, Hartford, Manchester, Meriden, Middletown, New Britain, New Haven, Norwalk, Norwich, Saybrook, Stamford, Torrington, Waterbury, and Willimantic. It is estimated that all the plans, which radiate from major centers of population, make a continuous emergency service available to more than 80% of Connecticut residents.

DISTRICT OF COLUMBIA

Neurology Training Grant.—The Georgetown University Medical Center, Washington, D. C., has received a neurology training grant of $189,645 from the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service. Dr. Francis M. Forster, dean of the Georgetown University School of Medicine and professor of neurology, who will administer the project, states that the neurology department expanded greatly under the impact of the original grant of $65,000 and that in the past five years the medical center has trained 20 young physicians in neurology.

FLORIDA

Fellowship in Cardiovascular Pathology.—A fellowship in cardiovascular pathology, established at the Mount Sinai Hospital of Greater Miami (4300 Alton Rd., Miami Beach 40) by the Bayshore Exchange Club of Miami Beach, offers a salary of $10,000 a year, with the expectation of continuance for two more years. Applicants must be board eligible or diplomates of the American Board of Pathology. The research, which will be related to congenital heart disease, the conduction system, and the pathology of the arteries and veins, will be carried out on a full-time basis in the research laboratories of the Mount Sinai Hospital under the direction of Dr. Maurice Lev.

ILLINOIS

Symposium on Cancer.—The 16th annual Symposium on Cancer will be presented under the sponsorship of the Illinois division, American Cancer Society, in conjunction with the Illinois State Medical Society, Feb. 1-3 at medical schools in Chicago. Among those who will lecture on Wednesday at Northwestern University Medical School and the University of Illinois College of Medicine are: Dr. Walter G. Maddock, professor of surgery, and Dr. Vincent J. O'Conor, head, department of urology, Northwestern University Medical School; Dr. Warren H. Cole, chairman, department of surgery; Dr. Paul H. Holinger, professor of bronchoesophagology, department of otolaryngology; and Dr. Danely P. Slaughter, associate professor of surgery and director, tumor clinic, Illinois Research Hospital, University of Illinois College of Medicine. Among the speakers on the program Thursday at Mercy Hospital, Stritch School of Medicine of Loyola University, and Michael Reese Hospital are: Dr. Warren W. Furey, assistant professor of radiology, and Dr. Herbert E. Schmitz, professor and chairman of the department of obstetrics and gynecology, Stritch School of Medicine of Loyola University; Dr. Alexander M. Buchholz, assistant professor of dermatology, University of Illinois College of Medicine; and Dr. Erich M. Uhlmann, assistant professor of radiology, Northwestern University School of Medicine. On Friday Dr. Dwight Edwin Clark, professor and secretary in the department of surgery, and Dr. C. Howard Hatcher, professor of orthopedic surgery, University of Chicago Medical School, will speak at the school.

Chicago

Monthly Cardiac Conference.—The monthly clinicopathological cardiac conference of Cook County Hospital will be held Feb. 10 from 11 a. m. to 12 noon in the Children's Amphitheater, 700 S. Wood St. "Pathogenesis and Treatment of Experimental Hypertensions" will be presented by Dr. George E. Wakerlin, professor of physiology, University of Illinois College of Medicine.

Course in Electrocardiography.—A graduate course in electrocardiographic interpretation will be given at Michael Reese Hospital by Dr. Louis N. Katz, director, cardiovascular department, Medical Research Institute, and associates, on 12 successive Wednesdays (7-9 p. m.) beginning Feb. 8. Information may be obtained from Mrs. Ana Rose, Medical Research Institute, Michael Reese Hospital, Chicago 16.

Medicolegal Lectures.—In its series, "The Physician Looks at Legal Problems," the Chicago Medical School (710 S. Wolcott Ave.) will present the following Tuesday lectures (12:30 p. m.):

Feb. 7, Chemical Tests for Intoxication, Sgt. Daniel T. Dragel, Scientific Crime Detection Laboratory, Chicago Police Department.

Feb. 14, Medicine and Law as Found in the Bible, Rabbi Louis Binstock, D.D., D.H.L., Temple Sholom.

Feb. 21, Insanity and the Law, Charles A. Bellows, J.D., attorney at law.

Heart Association Meeting.—The American Heart Association and the Chicago Heart Association will open the 1956 national campaign with a dinner program Jan. 31, 7 p. m., at the Palmer House. The speakers include Dr. Paul Dudley White, Boston, past-president of the American Heart Association; Dr. Louis N. Katz, president, Chicago Heart Association; and Dr. Irvine H. Page, president, American Heart Association, and director of research, Cleveland Clinic Foundation.

Dr. Lawless Honored.—Dr. Theodore K. Lawless was recently honored by Dillard University, New Orleans, which dedicated its newly erected half-million-dollar memorial chapel to Dr. Lawless and his father, the late Rev. Alfred Lawless, who "have given service to humanity through the Christian and medical ministries." Albert W. Dent, LL.D., president of the university, stated that Dr. Lawless had "made significant contributions, not only financial, but as vice-president of the school's trustee board." Dr. Lawless erected at his own expense and placed under university management the Gentilly Gardens Apartments for faculty members. The development, adjacent to the university, contains 12 modern buildings and 85 apartments.

IOWA

Eye Bank at the University.—The first eye bank in Iowa was recently established at the State University of Iowa Medical Center, Iowa City, with the support of the more than 250 Iowa Lions clubs. The eye bank, which is under the direction of Dr. Alson E. Braley, was made possible by a law passed at the winter session of the legislature, permitting persons to will parts of their body for medical use.

Personal.—The community of Renwick, in which Dr. Lee R. Turner has practiced for 47 years, recently honored him with a "Doctor Turner's Day." After a program in the high school auditorium, Dr. and Mrs. Turner were presented with luggage. ——Dr. Karl A. Catlin has succeeded Dr. Norman D. Render as superintendent of the Mental Health Institute, Clarinda, Dr. Render having moved to Norfolk, Neb. Dr. Catlin has been assistant to the superintendent.——Dr. James W. Culbertson, Iowa City, who recently participated in a graduate teaching program sponsored by the State Medical Society of Wisconsin, spoke at Rice Lake, Wisconsin Rapids, and at Appleton, on the current treatment of systemic arterial hypertension.——Dr. Robert C. Hardin, professor of internal medicine, State University of Iowa College of Medicine, Iowa City, has received a grant from the National Institutes of Health for the study of "Pathological Physiology in Juvenile Diabetics." Dr. Bernard I. Lewis, Iowa City, has received a grant from the Riker Laboratories, Inc., for the study of "The Cardiovascular Effects of Rauwolfia." Dr. Lewis recently addressed the Nebraska Heart

Association in Omaha on "The Use of Rauwolfia Serpentina in Patients with Coronary Artery Disease and Angina Pectoris." ——Dr. William B. Bean, Iowa City, recently participated in the National Vitamin Foundation Symposium at Vanderbilt University, Nashville, Tenn., and the meetings of the American Clinical and Climatological Society in Hot Springs, Va., and the American Association for the Study of Liver Disease and the Central Society for Clinical Research in Chicago. He was a guest teacher at Georgetown University Medical Center in Washington, D. C.——Dr. Alson E. Braley, head of the department of ophthalmology, State University of Iowa College of Medicine, Iowa City, has been appointed chairman of the ophthalmology training grant committee, National Institute of Neurological Diseases and Blindness, Bethesda, Md. Dr. Braley will develop a training program in ophthalmology to reduce the shortage of clinical teachers and investigators through grants made to teaching institutions.

LOUISIANA

Narcotic Violation.—Dr. Anthony Joseph Italiano, 6965 Vicksburg St., New Orleans, pleaded guilty on Oct. 6, 1955, in the U. S. District Court at New Orleans to a charge of violating the federal narcotic law. On Oct. 13 he was sentenced to serve a term of four years followed by a five-year period of probation and was fined $4,000.

Dr. Ochsner Honored.—Louisiana College, Pineville, recently honored Dr. Alton Ochsner, New Orleans, at its founder's day celebration, when it bestowed on him the seventh distinguished service award given by the college. Dr. Ochsner recently announced his intention to retire as chairman of the department of surgery at Tulane University of Louisiana School of Medicine after serving in that capacity since 1927. He will continue as a member of the faculty and as professor of clinical surgery.

Personal.—Dr. George E. Burch, chairman, department of medicine, Tulane University of Louisiana School of Medicine, New Orleans, has been elected a member of the American Board of Internal Medicine.——Dr. Rudolph J. Muelling Jr., New Orleans, was recently appointed pathologist to the Orleans parish coroner's office, replacing Dr. Stanley H. Durlacher, who left to become medical examiner for Dade County, Fla. Dr. Muelling is assistant director of pathology at Charity Hospital of Louisiana and assistant professor of pathology at the Louisiana State University School of Medicine.——Dr. Hiram O. Barker, former administrator and chief of radiology at Baptist Hospital, Alexandria, was honored by the board of administrators of the hospital on his retirement from the staff. A plaque presented to him was inscribed: "To Hiram O. Barker, M.D., administrator-radiologist emeritus, in grateful appreciation for 26 years' service to the Baptist Hospital. During the period of its early expansion as secretary of the medical staff for 25 years and as hospital administrator from 1934 to 1950, his foresight, wise counsel and untiring efforts were devoted to the service of humanity in the highest tradition of the profession. Presented by Baptist Hospital, November, 1955."

Graduate Medical Assembly.—The New Orleans Graduate Medical Assembly will hold its 19th annual meeting Feb. 27-March 1 in the Municipal Auditorium under the presidency of Dr. Donovan C. Browne, New Orleans. Guest speakers will include Dr. Philip D. Woodbridge, Greenfield, Mass.; Drs. J. Lowry Miller, Lawrence S. Kubie, and Arthur H. Blakemore, New York; Drs. Franz J. Ingelfinger, Duncan E. Reid, and Charles G. Child III, Boston; Drs. John I. Brewer, Claude N. Lambert, and Frank W. Newell, Chicago; Dr. S. Gilbert Blount Jr., Denver; Dr. Eugene A. Stead Jr., Durham, N. C.; Dr. John H. Talbott, Buffalo; Dr. Anderson C. Hilding, Duluth, Minn.; Dr. Alan R. Moritz, Cleveland; Dr. Joseph A. Johnston, Detroit; Dr. Philip J. Hodes, Philadelphia; and Dr. Rubin H. Flocks, Iowa City. At a joint meeting with the Orleans Parish Medical Society, 8 p. m., Dr. Blount will present "Primary Pulmonary Hypertension (Lantern Slides)," after which he, together with Dr. Moritz and Dr. Stead, will hold a clinicopathological conference. On Tuesday evening Dr. Blakemore will present "The Management of Hemorrhage from the Upper Gastrointestinal Tract, with Special Reference to Bleeding Esophageal Varices (Lantern Slides)," and Dr. G. Foard McGinnes, Washington, D. C., director of the vaccine program of the National Foundation for Infantile Paralysis, will have as his subject "The Present Status of Poliomyelitis Vaccine." The Wednesday morning session will open with a motion picture, "Sciatic Pain and the Intervertebral Disk," prepared for the bureau of medicine and surgery, U. S. Navy, and the Thursday session with a motion picture, "Cancer of the Thyroid" (American Cancer Society). Surgical and medical procedures will be televised daily in color.

The assembly has announced a postclinical tour of the West Indies and Central America, leaving March 2 for Puerto Rico, St. Thomas, Haiti, Jamaica, Panama, and Guatemala. Further information may be obtained from the assembly, 1430 Tulane Ave., New Orleans 12.

MAINE

Society News.—Newly elected officers of the Maine Society of Anesthesiologists include: Dr. Clement S. Dwyer, Bangor, president; Dr. Kenneth J. Cunco, Kennebunk, vice-president; and Dr. John R. Lincoln, Cumberland Center, secretary-treasurer.

MISSOURI

Society News.—At 8:30 p. m., Jan. 31, the St. Louis Medical Society will present a panel on E. coli diarrhea, with Dr. Alexis F. Hartmann, St. Louis, as moderator. The participants are Drs. John C. Herweg, M. Remsen Behrer, and J. Neal Middlekamp, and Helen Thornton, Ph.D.

Dr. Unterberg Honored.—At a testimonial dinner given for Dr. Hillel Unterberg, St. Louis, by the staff of Alexian Brothers Hospital, announcement was made that the department of neuropsychiatry would henceforth be known as the Hillel Unterberg Department of Neuropsychiatry.

Personal.—The Alumni Association of the St. Louis College of Pharmacy and Allied Sciences recently announced that the 1955 award for service to medicine will be bestowed on Dr. Evarts H. Graham, professor emeritus of surgery, Washington University School of Medicine, St. Louis, at the annual awards dinner of the Alumni Association, Feb. 26, at the Chase Hotel.

Medical Care for the Indigent.—A special committee has been named by the Missouri health council to recommend to its advisory committee on indigent care ways and means of developing a statewide program of medical care for indigent patients. Members of the special committee include Dr. James W. Colbert Jr., dean, St. Louis University School of Medicine; Dr. Roscoe L. Pullen, dean, University of Missouri School of Medicine, Columbia; and Dr. Archibald E. Spelman, chairman, committee on rural medicine, Missouri State Medical Association, Smithville.

NEW YORK

Society News.—Newly elected officers of the New York State Society of Industrial Medicine, Inc., include: Dr. Harold Brandaleone, president; Dr. Frank P. Guidotti, vice-president; and Dr. Harry E. Tebrock, secretary-treasurer, all of New York City.

Student Loan Fund.—The Jacobsen-Elsner Medical Society of Syracuse has contributed $250 to the J. J. Levy Memorial fund at State University of New York College of Medicine at Syracuse. The Levy fund was established by the Jacobsen-Elsner Society in memory of one of its founders, Dr. Jacob Joshua Levy, because of his interest in the problems of medical students. Dr. Levy was associate professor of medicine at the college at the time of his death in 1942.

Atomic Research Center.—The Atomic Energy Commission announces that an atomic medical research center will be constructed at the Brookhaven National Laboratory, which will have as its major installation a nuclear reactor specifically designed for medical research and treatment. The new center will also include a hospital designed primarily for research, an

industrial medicine branch, and research divisions in medical physics, pathology, microbiology, biochemistry, physiology, and clinical chemistry.

Appointed to Joint Post.—Dr. Jacob D. Goldstein, Rochester, who for 30 years has been affiliated with the University of Rochester School of Medicine and Dentistry, has been appointed to the joint post of professor of medicine, State University of New York College of Medicine at New York City, Brooklyn, and chief of medicine of its recent affiliate, the Jewish Hospital of Brooklyn. He will aid in developing the hospital as a training institution for the third and fourth year medical students at the college. Dr. Goldstein was a colonel in the Army Medical Corps during World War II. For three years after the war he was director of laboratories at Genesee Hospital, Rochester.

Memorial Professorship.—At a meeting in Rochester in memory of Dr. Albert D. Kaiser, city health officer, announcement was made of the establishment of a memorial professorship in public health and preventive medicine at the University of Rochester, where he had long served as professor of child hygiene in the school of medicine and as a member of the board of trustees. In eulogizing Dr. Kaiser, Cornelis W. de Kiewiet, Ph.D., president of the university, said, in part: "Ours is now the duty to turn his modesty into fame, his reticence into a living memorial, and his noble spirit into an enduring reminder of how a man can serve his God and his fellow man. . . ." Dr. Kaiser was a past-chairman of the A. M. A. Section on Pediatrics.

New York City

Lecture on Neoplastic Diseases.—On Feb. 3 at 3 p. m. "Some Tumor-Host Relationships" will be discussed by Dr. G. Borroughs Mider, associate director in charge of research, National Cancer Institute, Bethesda, Md., in the west basement conference hall at Montefiore Hospital.

Memorial Fund.—Colleagues and friends of the late Dr. Thomas T. Mackie have established a fund in his name at the Roosevelt Hospital, to be used in connection with the Thomas T. Mackie Memorial Library. Contributions may be sent to the Roosevelt Hospital, New York 19.

Lecture to the Laity.—In its 21st series of lectures to the laity the New York Academy of Medicine, 2 E. 103rd St., will present "Acculturation in Relation to the Concepts of Health and Disease" by Raymond W. Firth, Ph.D., head of the department of anthropology, London School of Economics and Political Science, University of London, England, Feb. 1, 8:30 p. m.

Hospital News.—The Hospital for Special Surgery recently received 1½ million dollars for construction of the Alfred H. Caspary Research Building at East 71st Street and East River Drive. The gift is part of 2½ million dollars in contributions from the estate of the late Mr. Caspary. In addition, a $200,000 gift from the Alfred H. and Margaret M. Caspary Foundation has been received, and a 3-million-dollar trust fund was set up for the hospital by the late Helen G. Bicknell of Findlay, Ohio.

Society News.—At its annual meeting Jan. 5, the New York Academy of Medicine presented the academy plaque to Dr. Malcolm Goodridge, past-president, and the academy medal to Dr. Eugene F. DuBois, formerly professor of physiology and biophysics at Cornell University Medical College. The anniversary discourse on Public Health in the Future was delivered by Dr. Herman E. Hilleboe, commissioner of health, State of New York. Dr. Harold B. Keyes, director of surgery at French Hospital, was elected vice-president of the academy.

Symposium on Crash Prevention.—The Hermann M. Biggs Memorial Lecture of the New York Academy of Medicine will be presented Feb. 2, 8:30 p. m., as a symposium on "Automobile Accidents and Their Prevention." There will be no admission fee. Mr. John O. Moore, director, automotive crash injuries research project, which has been under way for several years in the department of preventive medicine and public health at Cornell University Medical College, will describe the epidemiology of automobile accidents. Dr. Herbert J. Stack, director, Center for Safety Education at New York University, where studies of the human element in accidents have been carried on for 10 years, will consider "The Psychology of Drivers." Traffic conditions will be discussed by Paul H. Blaisdell, director, traffic safety division, Association of Casualty and Surety Companies, New York, and New York's commissioner of traffic, T. T. Wiley, will discuss the engineering features involved in the traffic situation in New York.

Medical College Dedicated.—The Albert Einstein College of Medicine of Yeshiva University was recently dedicated at Morris Park Avenue and Eastchester Road in the East Bronx. A plaque, presented by the college's first class of 53 young men and 3 young women, to Hans Albert Einstein, Ph.D., son of the late Prof. Albert Einstein, was inscribed with a pledge that the students would "carry on in the spirit of warm humanity and scientific integrity exemplified by Albert Einstein, justifying his high hopes for the college as a valuable instrument for advancing medical science and the national welfare." The school is the newest unit of a 100-million-dollar medical center, to which the city has already contributed the 511-bed Nathan B. Van Etten Hospital, opened in 1954. A 45-million-dollar psychiatric hospital, to be erected by the state, on a 124-acre site along the Hutchinson River Parkway, will be another unit in the center. The college, the first medical college to be established in this country under Jewish auspices, will choose its students and faculty without reference to race, creed, or national origin.

Personal.—Dr. Leona Baumgartner, commissioner of the New York City Department of Health, recently visited India at the invitation of the minister for health. She was asked to act as consultant to the Indian Ministry for Health on health problems, particularly those of maternal and child health.——Dr. George T. Pack will speak about "Moles and Melanomas" before the Royal Australasian College of Surgeons at their meeting in Christchurch, New Zealand, Feb. 1-4. He will also deliver an invitational series of graduate lectures at the University of Sydney, Australia.——Dr. Wilson G. Smillie, who recently retired as professor of public health and preventive medicine at the Cornell University Medical College, has been appointed executive director of the State Charities Aid Association, a voluntary statewide agency for the improvement of health and welfare conditions, to succeed Dr. Harry S. Mustard, who has retired after six years as executive director.——Dr. Arthur Bitrin, assistant clinical professor of psychiatry, New York University College of Medicine, has been appointed director of the psychiatric service of Bellevue Hospital Center, succeeding Dr. Lewis I. Sharp, director for the past seven years, who will continue on the teaching staff of the department of psychiatry. Dr. Zitrin has been with the staff of New York University-Bellevue Medical Center since 1948.

OHIO

Aaron Brown Lectureship.—The Chi chapter of **Phi** Delta Epsilon fraternity at the Ohio State University College of Medicine, Columbus, will hold its sixth annual Aaron Brown Lectureship Feb. 1. Dr. Harry Goldblatt of Mount Sinai Hospital, Cleveland, will discuss "Experimental Cancer."

Residency in Allergy.—An accredited residency in allergy will be available at the Ohio State University Health Center, Columbus, July 1. Facilities include inpatients and outpatients and clinical and private services, with opportunity for experience in related specialities. For details, write Dr. John H. Mitchell, 1625 Perry St., Columbus 1.

Personal.—Dr. Hilda R. Knobloch, formerly assistant professor in the division of maternal and child health, Johns Hopkins University School of Hygiene and Public Health, Baltimore, has been appointed to the staff of the Children's Hospital, Columbus, as associate professor of pediatrics at the Ohio State University College of Medicine, Columbus. She will devote most of her time to teaching and research in the problems of development in infancy and the preschool years.——Dr. Leslie T. Webster Jr., demonstrator in medicine, Western Reserve University School of Medicine, Cleveland, has been awarded the second Russell M. Wilder fellowship to be granted by the National

Vitamin Foundation. Dr. Webster, also an assistant visiting physician at City Hospital, Cleveland, will continue his studies of the metabolism of protein, amino acids, and ammonium in patients with and without liver disease. The three-year fellowship, established in 1953, carries a stipend of $15,000 and is granted annually.

Medicolegal Institute.—"The Back: A Law-Medicine Problem" will be the theme of an institute, Feb. 3-4, at the Western Reserve University School of Law, Cleveland. Institute co-chairmen are Oliver C. Schroeder Jr., director of the Law-Medicine Center, and Dr. Samuel R. Gerber, Cleveland, Cuyahoga County coroner. The topics on Friday will be: functional anatomy of the back; x-ray and the back—what it can prove; congenital variations of structure of the spine and susceptibility to injury; diseases of the back predisposing to or simulating injury; fracture of the spine; whiplash injuries of the neck; the orthopedic surgeon and intervertebral disks—differential diagnosis; and soft-tissue injuries to the back. Saturday's lectures will concern: neurological and psychiatric aspects of back injury; effect of injury on the arthritic spine; and medical evaluation of the back injury. Sessions are scheduled for morning and afternoon of each conference day. Registration, $25 payable in advance. Information on the institute and on other programs of the university's legal medicine agency is available from: Oliver C. Schroeder Jr., Director, Law-Medicine Center, Western Reserve University, Cleveland 6.

SOUTH DAKOTA

Society News.—Newly elected officers of the South Dakota Society of Internal Medicine include: Dr. Jack Donahoe, Sioux Falls, president; Dr. Donald L. Kegaries, Rapid City, vice-president; and Dr. Warren L. Jones, Sioux Falls, secretary-treasurer.

Personal.—Dr. Frank C. Totten, Lemmon, has been appointed to the South Dakota Health Advisory Council of the state department of health. Dr. Totten will fill the unexpired term of Dr. Roscoe E. Dean Jr. of Wessington Springs, which runs until 1957.——Dr. Anthony E. Coletti, recently clinical director at Central State Hospital, Lakeland, Ky., has become assistant superintendent at Yankton State Hospital.——F. Ellis Kelsey, Ph.D., University of South Dakota School of Medical Sciences, Vermillion, has received a renewal of a research grant from the American Heart Association in the amount of $5,250 to permit a continuation of his study on the action of radioactive digitoxin.

TENNESSEE

Personal.—Dr. Rudolph H. Kampmeier, professor of medicine, Vanderbilt University School of Medicine, Nashville, was the annual physician-in-chief pro tempore, Dec. 15-17, 1955, at the Cleveland (Ohio) Clinic, where he devoted his time to the teaching program of the fellows in medicine.

University News.—The University of Tennessee College of Medicine, Memphis, has appointed as assistants: Dr. Prentiss A. Turman, division of obstetrics and gynecology; Dr. Joseph H. Brock, division of surgery; and Dr. Marvin L. Wolff, division of medicine.

Brooks Lecture.—The Barney Brooks Lecture was delivered at the Vanderbilt University School of Medicine Amphitheater, Nashville, Jan. 20, by Dr. Emile F. Holman, professor emeritus, Stanford University School of Medicine, San Francisco, on "Significance of Segmental Stenosis and Poststenotic Dilatation in the Development of Arterial Aneurysms."

Visiting Lecturer.—On Jan. 26-28 Dr. A. Murray Fisher, associate professor of medicine, Johns Hopkins University School of Medicine, Baltimore, participated in a clinicopathological conference and ward rounds at Vanderbilt University School of Medicine, Nashville, where he also lectured on "Pulmonary Disease, Particularly in Nontuberculosis Infection in Relation to the Development of Cardiopulmonary Disease."

TEXAS

Pediatric Conference.—The University of Texas School of Medicine, Galveston, will hold a pediatric postgraduate conference, Feb. 9-11. The speakers will include Drs. Leo Kanner, Baltimore; Haddow M. Keith, Minneapolis; Herbert C. Miller, Kansas City, Kan.; James L. Dennis, Oakland, Calif.; Clifford G. Grulee Jr., New Orleans; and Vincent Charles Kelley, Salt Lake City.

HAWAII

Society News.—Newly elected officers of the Honolulu Pediatric Society include: Dr. Douglas H. Murray, Honolulu, president; Dr. William F. Moore, Honolulu, recording secretary; and Dr. Duke Cho Choy, Honolulu, corresponding secretary-treasurer.

GENERAL

Meeting of Medical Librarians.—The midwest regional group of the Medical Library Association will hold its midwinter meeting Feb. 3, 7:30 p. m., in the Northwestern University Dental School Library, 10th Floor, 311 E. Chicago Ave., Chicago. "Medical Literature and Medical Education" will be discussed by Dr. Harry Sicher, Loyola University, Chicago College of Dental Surgery. Dinner, preceded by cocktails, is planned at the Normandy House Restaurant, 800 N. Michigan Ave., at 5:30 p. m.

Muscular Dystrophy Research.—Muscular Dystrophy Associations of America, Inc. (39 Broadway, New York 6) announces that between March 31, 1954, and Oct. 1, 1955, research grants-in-aid were made to 63 scientists in 25 states and to 4 abroad. Since the organization was founded in June, 1950, it has received funds totaling $9,179,274 and, of this amount, has allocated to research and patient care nearly 6 million dollars, or 63.1%. Dr. Ade T. Milhorat, New York, is chairman of the medical advisory board.

Awards in Dermatology.—The American Dermatological Association announces the following winners of its annual essay prize contest: first prize, $500, to Dr. Alfred W. Kopf, New York, "Histo-Chemical Studies on the Distribution of Alkaline Phosphatase in Normal and Pathologic Human Skin," which he has been invited to present at the annual meeting of the American Dermatological Association in Santa Barbara, Calif., June 18-21; second prize, $400, to Drs. James F. Riley and B. G. West, Dundee, Scotland, for "Skin Histamines: Location in the Tissue Mast Cells"; third prize, $300, to Dr. John G. Rukavina, Ann Arbor, Mich., for "Familial Primary Systemic Amyloidosis. An Experimental, Genetic and Clinical Study"; and fourth prize, $200, to Dr. John S. Strauss, Philadelphia, for "Pseudofolliculitis of the Beard."

Meeting of Anesthesiologists.—At its meeting Feb. 3 the New England Society of Anesthesiologists will present the following program at 2:15 p. m. in the Joslin Auditorium, New England Deaconess Hospital, Boston:

Tracheobronchial Aspiration, Robert B. Orr, Lahey Clinic, Boston.
Complications of Endotracheal Anesthesia, Stewart A. Wilber, Newton-Wellesley Hospital, Newton Lower Falls, Mass.
The Diabetes Patient, Robert F. Bradley, Joslin Diabetic Clinic, Boston.

A cocktail hour (5 p. m.), dinner, and business meeting will precede the evening session at Longwood Towers, Boston, at which "Myelaxin, Pharmacological Aspects and Clinical Evaluation" will be discussed by C. J. Cavallito, Ph.D., director of research division, Irwin-Neisler and Company, and Dr. Julia G. Arrowood, director, department of anesthesiology, Massachusetts Memorial Hospitals, Boston.

Society News.—Dr. Donald L. Paulson, Dallas, Texas, was recently elected president of the **Southern Thoracic Surgical Association;** Dr. Edward F. Parker, Charleston, S. C., vice-president; and Dr. Hawley H. Seiler, Tampa, Fla., secretary-treasurer (reelected).——Current officers of the **Society of Nuclear Medicine** include: Dr. Milo T. Harris, Spokane, Wash., president; Norman J. Holter, M.S., Helena, Mont., president-elect;

Dr. Robert G. Moffat, Vancouver, Canada, secretary; and R. Labbe, Ph.D., Portland, Ore., treasurer. The 1956 meeting will be held at the Hotel Utah, Salt Lake City, June 21-23.—— Newly elected officers of the **American Association of Blood Banks** include: Dr. Ernest E. Muirhead, Dallas, Texas, president-elect; Dr. Ralph M. Hartwell, New Orleans, vice-president; Miss Marjorie Saunders, LL.B., Dallas, Texas, secretary; and Mrs. Bernice M. Hemphill, San Francisco, treasurer (reelected). Dr. James J. Griffitts, Miami, Fla., is president.

American Nuclear Society.—The American Nuclear Society, which has built a membership of more than 1,000 since its incorporation in January, 1955, will publish the first issue of its bimonthly journal, *Nuclear Science and Engineering*, in February. The society on Dec. 13, 1955, granted a charter to the University of Michigan student branch, making it the first of the society's student affiliate section. Henry J. Gomberg, Ph.D., is faculty advisor for the group. Formal installation ceremonies will be held during the spring semester; Walter H. Zinn, Ph.D., director of Argonne National Laboratory, Lemont, Ill., and president of the society, will deliver the installation address. Membership is open to physicists, chemists, mathematicians, biologists, physicians, and engineers engaged in professional activity in one or more fields of nuclear science or engineering. Information may be obtained from the Executive Secretary, American Nuclear Society, Box 963, Oak Ridge, Tenn.

Dr. Davison Honored.—Dr. Hal M. Davison, Atlanta, Ga., president-elect of the Medical Association of Georgia, recently served as toastmaster and as co-chairman of the Atlanta Round

Dr. Davison (right) and co-chairmen welcome Miss Cornelia Otis Skinner.

Table of the National Conference of Christians and Jews in welcoming Miss Cornelia Otis Skinner to Atlanta for a luncheon meeting of the organization. Miss Skinner's topic was "What You and I Can Do for Brotherhood."

Fellowship in Dermal Pathology.—This fellowship, sponsored by the American Academy of Dermatology and Syphilology, provides opportunity for study in dermal pathology to a postgraduate student who has completed at least one year, preferably two, of training in dermatology. The stipend is $4,000 a year. A period of training will be spent at the Armed Forces Institute of Pathology, Washington, D. C., the appointment being subject to approval by the director of the institute. The American Board of Dermatology and Syphilology has approved the institute for one year of training, but the student must complete one year of graduate training either before or after completion of the Osborne fellowship, in an institution approved by the board for three years of training. Application blanks may be obtained from Dr. Hamilton Montgomery, chairman of the committee on pathology of the American Academy of Dermatology and Syphilology, 200 First St. S. W., Rochester, Minn. The next available appointment begins July 1, 1957. Early application is urged, and, as a rule, applications will not be considered after Sept. 1, 1956, for the July 1, 1957, appointment.

Training in Child Psychiatry.—This training is available in a number of member clinics approved as training centers by the American Association of Psychiatric Clinics for Children. The training begins at a third year, postgraduate level with the following minimum prerequisites: graduation from an approved medical school, an approved general or rotating internship, and a two-year residency in psychiatry, approved by the American Board of Psychiatry and Neurology. Most of these clinics have also been approved individually by the American Board of Psychiatry and Neurology for a third year of training and for an additional year of experience. This training is in preparation for specialization in child psychiatry and especially for positions in community clinics. Fellows receive instruction in therapeutic techniques with children in outpatient settings that utilize the integrated services of the psychiatric clinic team. Most of the clinics have a two-year training period. Fellowship stipends are usually about $3,600. Applications may be made either through the office of the American Association of Psychiatric Clinics for Children or directly to the individual clinics. For information write Miss Marion A. Wagner, Administrative Assistant, American Association of Psychiatric Clinics for Children, 1790 Broadway, Room 916, New York 19.

Meeting of Allergists.—The American Academy of Allergy will hold its 12th annual meeting Feb. 4-8 at the Chase and Park Plaza hotels, St. Louis. "Indications and Contraindications for Therapy in Bronchial Asthma" will be presented as a panel at 9 a. m. Saturday, with Dr. Leo H. Criep, Pittsburgh, as moderator. Panelists will be Drs. Harry L. Alexander and Samuel C. Bukantz, St. Louis; Alvan L. Barach, New York; Thaddeus S. Danowski, Pittsburgh; Louis Weinstein, Boston; and John C. Krantz Jr., Ph.D., Baltimore. At 2 p. m. a panel, "Immunological and Clinical Aspects of Antigen Therapy," will be presented, with Dr. Oscar Swineford, Charlottesville, Va., as moderator, and Drs. J. Harvey Black, Dallas, Texas, Samuel M. Feinberg, Chicago, and William B. Sherman, New York, as participants. On Sunday morning the Association of Allergists for Mycological Investigations will present a program on research problems currently under study and phases of clinical mold allergy. In the afternoon the academy will offer a panel discussion, "Pediatric Allergy," with Dr. Charles A. Janeway, Boston, as moderator. Participants will be Drs. Harry S. Bernton, Washington, D. C.; Ralph Bowen, Houston, Texas; Vincent J. Derbes, New Orleans; Harry L. Mueller, Winchester, Mass.; James C. Overall, Nashville, Tenn.; and Donald L. Thurston, St. Louis. Physicians are invited to attend the session. There is no registration fee.

FOREIGN

Course in Pediatric Psychiatry.—The summer school of the University of Vienna (St. Wolfgang Campus, Strobl, Austria) will offer a 30-hour course, "The Biological Basis of Child Psychology and Child Psychiatry," July 15-Aug. 4 under the chairmanship of Prof. Dr. Hans Asperger, School of Medicine, University of Vienna. Topics to be considered include: Basic Problems of Child Psychiatry from the Biological Point of View; General Biological Laws Concerning the Function of the Central Nervous System; Importance of the Bodily Constitution and of the Environment for the Development of Disorders and Social Behavior; Psychopathology of Childhood and Adolescence, Forms of Juvenile Delinquency; and Pedagogical Therapy of Mental and Social Disturbances. Special requirements: at least two years basic psychology, teachers' college, psychology in medical schools or law schools (juvenile psychology).

Seminar Congresses in Obstetrics and Gynecology.—In its seminar congresses in obstetrics and gynecology, the American Medical Society of Vienna, Austria, will present the following programs by the medical faculty of the University of Vienna:

April 19-21, Vaginal Operative Approach of Pelvis.
May 17-19, Gynecological Pathology; Gynecological Endocrinology; Gynecological Cytology.
June 21-23, Manikin Obstetrics.
July 19-21, Gynecology; Oncology; Female Urology.
Aug. 23-25, Sterility; Fertility; Hormone Therapy.
Sept. 20-22, Surgical Obstetrics; Manikin Obstetrics; Operative Gynecology.
Oct. 25-27, Gynecologic Surgery; Wertheim Approach; Obstetrical Surgery.

Details may be obtained from the American Medical Society of Vienna, Vienna I., Universitaetsstrasse 11, Cable: "Ammedic" Vienna.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1956 Annual Meeting, Chicago, June 11-15.

1956 Clinical Meeting, Seattle, Nov. 27-30.

1957 Annual Meeting, New York, June 3-7.

1957 Clinical Meeting, Philadelphia, Dec. 3-6.

1958 Annual Meeting, San Francisco, June 23-27.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE, Palmer House, Chicago, Feb. 11-14. Dr. Edward L. Turner, 535 N. Dearborn St., Chicago 10, Secretary.

NATIONAL CONFERENCE ON RURAL HEALTH, Multnomah Hotel, Portland, Ore., Mar. 8-10. Mrs. Arline Hibbard, 535 N. Dearborn St., Chicago 10, Secretary.

ALASKA TERRITORIAL MEDICAL ASSOCIATION, Alaska Native Health Service Hospital, Anchorage, Feb. 20-22. Dr. Robert B. Wilkins, 1121 Fourth Ave., Anchorage, Secretary.

AMERICAN ACADEMY OF ALLERGY, Chase Hotel, St. Louis, Feb. 6-8. Dr. Francis C. Lowell, 65 East Newton St., Boston, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Drake Hotel, Chicago, Feb. 23-25. Dr. Walter J. Camp, 1853 West Polk St., Chicago, Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, Hotel Statler, Washington, D. C., Mar. 19-22. Mr. Mac F. Cahal, Broadway at 34th Street, Kansas City 11, Mo., Executive Secretary.

AMERICAN ACADEMY OF OCCUPATIONAL MEDICINE, Netherlands-Plaza Hotel, Cincinnati, Feb. 15-17. Dr. Leonard J. Goldwater, 600 W. 168th St., New York 32, Secretary.

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, Palmer House, Chicago, Jan. 28-Feb. 2. Dr. John R. Norcross, 122 South Michigan Blvd., Chicago 3, Secretary.

AMERICAN ASSOCIATION FOR HEALTH — PHYSICAL EDUCATION, RECREATION, Conrad Hilton Hotel, Chicago, Mar. 24-30. Mr. Carl A. Troester Jr., 1201 Sixteenth St., N.W., Washington 6, D. C., Executive Secretary.

AMERICAN COLLEGE OF RADIOLOGY, Drake Hotel, Chicago, Feb. 10-11. Mr. William C. Stronach, 20 North Wacker Drive, Chicago 6, Executive Secretary.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION, Hotel Commodore, New York, Mar. 15-17. Dr. Marion F. Langer, 1790 Broadway, New York 19, Executive Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Sheraton Plaza, Boston, Mar. 24-25. Dr. Theodore Lidz, 333 Cedar St., New Haven 11, Conn., Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Jung Hotel, New Orleans, Mar. 18-21. Dr. John A. Drummond, 1414 Drummond St., Montreal, Canada, Secretary.

CENTRAL SURGICAL ASSOCIATION, Hotel Kahler, Rochester, Minn., Feb. 23-25. Dr. Charles D. Branch, 102 North St., Peoria, Ill., Secretary.

CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer House, Chicago, Feb. 28-March 2. Dr. Norris J. Heckel, 86 E. Randolph St., Chicago 1, Secretary.

DALLAS SOUTHERN CLINICAL SOCIETY, Dallas, Tex., Mar. 12-14. Miss Helga Boyd, 433 Medical Arts Bldg., Dallas 1, Tex., Executive Secretary.

EASTERN CONFERENCE OF RADIOLOGISTS, Lord Baltimore Hotel, Baltimore, Mar. 15-17. Dr. Richard B. Hanchett, 705 Medical Arts Bldg., Baltimore 1, Secretary.

MEDICAL SOCIETY EXECUTIVES CONFERENCE, Drake Hotel, Chicago, Feb. 6-8. Mr. H. Martin Baker, 1102 South Hillside, Wichita 17, Kansas, Secretary.

MICHIGAN CLINICAL INSTITUTE, Sheraton-Cadillac Hotel, Detroit, Mar. 7-9. Dr. L. Fernald Foster, 606 Townsend St., Lansing 15, Secretary.

MICROCIRCULATORY CONFERENCE, Hotel Schroeder, Milwaukee, Apr. 3. Dr. George P. Fulton, Boston University, Dept. of Biology, 675 Commonwealth Ave., Boston 15, Chairman.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, Feb. 27-March 1. Dr. Eugene H. Countiss, Room 103, 1430 Tulane Ave., New Orleans 12, Director.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:

SASKATOON, SASK., Feb. 3-4. Dr. C. H. A. Walton, Winnipeg Clinic, Winnipeg, Man., Canada, Governor.

TUCSON, ARIZ., Feb. 11. Dr. Leslie R. Kober, 15 East Monroe St., Phoenix, Ariz., Governor.

LINCOLN, NEB., Cornhusker Hotel, Mar. 3. Dr. Edmond M. Walsh, 1412 Medical Arts Bldg., Omaha 2, Neb., Chairman.

KANSAS CITY, KANS., Mar. 23. Dr. William C. Menninger, 317 West 6th Ave., Topeka, Kans., Governor.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:

PHILADELPHIA, The Bellevue-Stratford, Feb. 13-16. Dr. Calvin M. Smyth Jr., Abington Memorial Hospital, Abington, Pa., Chairman.

MILWAUKEE, Hotel Schroeder, Feb. 27-29. Dr. Forrester Raine, 425 E. Wisconsin Ave., Milwaukee 4, Chairman.

COLORADO SPRINGS, COLO., The Broadmoor, Mar. 5-7. Dr. George W. Bancroft, 106 E. St. Vrain St., Colorado Springs, Colo., Chairman.

LITTLE ROCK, ARK., Hotel Marion, Mar. 12-13. Dr. Joseph F. Shuffield, 103 E. 7th St., Little Rock, Ark., Chairman.

SOCIETY OF UNIVERSITY SURGEONS, Hotel Claypool, Indianapolis, Feb. 8-10. Dr. C. Rollins Hanlon, 1325 South Grand Blvd., St. Louis 4, Secretary.

SOUTH ATLANTIC ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS, Hollywood Beach Hotel, Hollywood, Fla., Jan. 28-Feb. 1. Dr. C. H. Mauzy, Bowman Gray School of Medicine, Winston-Salem, N. C., Secretary.

SOUTHEASTERN SURGICAL CONGRESS, John Marshall Hotel, Richmond, Va., Mar. 12-15. Dr. Benjamin T. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.

SOUTHERN NEUROSURGICAL SOCIETY, George Washington Hotel, Jacksonville, Fla., Mar. 23-24. Dr. William F. Meacham, Vanderbilt University Hospital, Nashville 5, Tenn., Secretary.

U. S. SECTION, INTERNATIONAL COLLEGE OF SURGEONS, REGIONAL MEETING, Greenbrier Hotel, White Sulphur Springs, W. Va., Feb. 12-15. Dr. E. G. Gill, 711 South Jefferson St., Roanoke, Va., Chairman.

FOREIGN AND INTERNATIONAL

ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS, London School of Hygiene and Tropical Medicine, London W.C.1, England, Sept. 24-28, 1956. Dr. J. A. A. Mekelburg, Peek, Frean and Company, Ltd., Keetons Rd., Bermondsey, London, S.E.16, England, Honorable Secretary.

BRITISH MEDICAL ASSOCIATION, Brighton, England, July 9-13, 1956. Dr. Angus Macrae, B. M. A. House, Tavistock Square, London, W.C.1, England.

CANADIAN MEDICAL ASSOCIATION, Quebec, P. Q., Canada, June 10-14, 1956. Dr. Arthur D. Kelly, 150 St. George St., Toronto 5, Ont., Canada, Secretary.

CONFERENCE OF INTERNATIONAL UNION FOR HEALTH EDUCATION OF THE PUBLIC, Rome, Italy, April 27-May 5, 1956. Mr. Lucien Viborel, 92 rue St. Denis, Paris 1er, France, Secretary-General.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Miami Beach, Fla., U.S.A., April 9-12, 1956. For information write: Dr. R. J. Whitacre, 13951 Terrace Road, Cleveland 12, Ohio, U. S. A.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LIMNOLOGY, Helsinki, Finland, July 26-Aug. 7, 1956. For information address: Dr. H. Luther, Snellmansgatan 16 C 36, Helsinki, Finland.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LOGOPEDICS AND PHONIATRICS, Barcelona, Spain, Sept. 3-7, 1956. Dr. J. Perello, Provenza 319, Barcelona 9, Spain, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF HEMATOLOGY, Hotel Somerset, Boston, Mass., U.S.A., Aug. 27-Sept. 1, 1956. Dr. W. C. Moloney, 39 Bay State Road, Boston, Mass., U.S.A., Secretary.

CONGRESS OF INTERNATIONAL UNION AGAINST TUBERCULOSIS, New Delhi, India, Jan. 3-6, 1957. For information address: Secretariat, The Union, 66 Boulevard Saint-Michel, Paris 6e, France.

CONGRESS OF LATIN SOCIETY OF OPHTHALMOLOGY, Madrid, Spain, April 24-28, 1956. For information address: Dr. Costi, Montalban 3, Madrid, Spain.

EUROPEAN CONGRESS OF ALLERGOLOGY, Florence, Italy, Sept. 12-15, 1956. Prof. Umberto Serafini, Instituto de Patologia Medica, Viale Morgagni, Florence, Italy, Secretary-General.

EUROPEAN CONGRESS OF CARDIOLOGY, Stockholm, Sweden, Sept. 10-14, 1956. Dr. Karl Erik Grewin, Sodersjukhuset, Stockholm, Sweden, General Secretary.

EUROPEAN SYMPOSIUM ON VITAMIN B_{12}, Hamburg, Germany, May, 1956. For information write: Doz. Dr. H. Bauer, Nervenklinik, Hamburg-Eppendorf, Germany.

HEALTH CONGRESS, ROYAL SOCIETY FOR THE PROMOTION OF HEALTH, Blackpool, England, April 24-27, 1956. Mr. P. Arthur Wells, 90 Buckingham Palace Road, London S.W. 1, England, Secretary.

INTER-AMERICAN CONGRESS OF CARDIOLOGY, Havana, Cuba, Nov. 4-10, 1956. For information address: Dr. Ramon Aixala, Apartado 2108, Havana, Cuba.

INTERNATIONAL ACADEMY OF PATHOLOGY, Cincinnati, Ohio, U. S. A., April 24-25, 1956. Dr. F. K. Mostofi, Armed Forces Institute of Pathology, Washington 25, D. C., U. S. A., Secretary.

INTERNATIONAL CONGRESS AGAINST ALCOHOLISM, Istanbul, Turkey, Sept. 10-15, 1956. For information address: International contre l'Alcoolisme, Case Gare 49, Lausanne, Switzerland.

INTERNATIONAL CONGRESS ON ANIMAL REPRODUCTION, Arts School, University of Cambridge, Cambridge, England, June 25-30, 1956. Dr. Joseph Edwards, Production Division, Milk Marketing Board, Thames Ditton, Surrey, England, Hon. Secretary.

INTERNATIONAL CONGRESS OF ANTHROPOLOGICAL AND ETHNOLOGICAL SCIENCES, Philadelphia, Pa., U. S. A., Sept. 2-9, 1956. Dr. William N. Fenton, National Research Council, Division of Anthropology and Psychology, 2101 Constitution Avenue, Washington 25, D. C., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF DIETETICS, Congress Palace, Esposizione Universale Roma, Rome, Italy, Sept. 10-14, 1956. Prof. E. Serianni, Associazione Dietetica, Italiana, via dei Penitenzieri N. 13, Rome, Italy, Secretary General.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Cologne, Germany, Aug. 19-23, 1956. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, U. S. A., Executive Director.

INTERNATIONAL CONGRESS OF ENTOMOLOGY, Montreal, Canada, Aug. 17-25, 1956. Mr. J. A. Downes, Science Service Bldg., Carling Ave., Ottawa, Ont., Canada, Secretary.

INTERNATIONAL CONGRESS OF GASTROENTEROLOGY, London, England, July 18-21, 1956. Mr. Hermon Taylor, London Hospital, White Chapel, London E.1, England, Honorable Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Maison de la Mutualite, Paris, France, June 5-8, 1956. For information address: Mr. M. H. Thoillier, 37 Rue de Monthlon, Paris 9e, France.

INTERNATIONAL CONGRESS FOR THE HISTORY OF SCIENCE, Florence and Milan, Italy, Sept. 3-10, 1956. Dr. M. L. Bonelli, Instituto di Ottica, Arcetri, Florence, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF HUMAN GENETICS, Copenhagen, Denmark, Aug. 1-6, 1956. For information address: The University Institute for Human Genetics, Tagensvej 14, Copenhagen N, Denmark.

INTERNATIONAL CONGRESS OF HYDATID DISEASE, Athens, Greece, Sept. 14-18, 1956. Prof. B. Kourias, Croix-Rouge Hellenique, 1 rue Mackenzie King, Athens, Greece, Secretary-General.

INTERNATIONAL CONGRESS ON INFECTIOUS PATHOLOGY, Lyon, France, May 24-26, 1956. General Secretariat: Institut Pasteur de Lyon, 77 rue Pasteur, Lyon, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Madrid, Spain, Sept. 19-23, 1956. Dr. J. C. De Oya and Dr. J. Gimena, Hostaleza No. 90, Madrid, Spain, Secretaries.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Palmer House, Chicago, Illinois, U. S. A., Sept. 9-13, 1956. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, Shoreham Hotel, Washington, D. C., U. S. A., Oct. 1-5, 1956. For information address: Miss Doris Gleason, Executive Director, American Association of Medical Record Librarians, 510 North Dearborn St., Chicago 10, Illinois, U. S. A.

INTERNATIONAL CONGRESS OF NEO-HIPPOCRATIC MEDICINE, Montecatini, Terme, Italy, May 20-22, 1956. Dr. Valente, 41 Avenue Verdi, Montecatini Terme, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Copenhagen, Denmark, July 22-27, 1956. Professor P. Plum, Rigshospitalet, Copenhagen, Denmark, President.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, Copenhagen, Denmark, August 20-24, 1956. Dr. B. Strandberg, Kobenhavns amts sygehus i Gentofte, Dept. of Rheumatology and Physical Medicine, Hellerup, Denmark, Honorable Secretary.

INTERNATIONAL CONGRESS OF RADIOLOGY, Mexico, D. F., Mexico, July 22-28, 1956. Dr. Jose Noriega, Tepic 126 (2e piso), Mexico, D. F. 7, Mexico, Secretary General.

INTERNATIONAL CONGRESS OF WORLD CONFEDERATION FOR PHYSICAL THERAPY, Hotel Statler, New York, New York, U. S. A., June 17-23, 1956. For information address: Miss Mildred Elson, American Physical Therapy Association, 1790 Broadway, New York 19, New York, U. S. A.

INTERNATIONAL GENETICS SYMPOSIUM, Tokyo and Kyoto, Japan, Sept. 6-12, 1956. For information address: Secretary, International Genetics Symposium, Science Council of Japan, Ueno Park, Tokyo, Japan.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Brussels, Belgium, July 29-Aug. 5, 1956. For information address: Prof. J. Reuse, Faculte de Medicine et de Pharmacie, 115 Boulevard de Waterloo, Brussels, Belgium.

INTERNATIONAL PROFESSIONAL UNION OF GYNECOLOGISTS AND OBSTETRICIANS, Madrid, Spain, Sept. 28-29, 1956. Dr. Jacques Courtois, 1 rue Racine, St-Germain-en-Laye (S and O), France, Permanent International Secretary-General.

INTERNATIONAL SYMPOSIUM ON VENEREAL DISEASES AND THE TREPONEMATOSES, Hotel Statler, Washington, D. C., U. S. A., May 28-June 1, 1956. For information address: Dr. Charles A. Smith, Chief, Venereal Disease Program, Division of Special Health Services, Public Health Service, Dept. of Health, Education and Welfare, Washington 25, D. C., U. S. A.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, San Juan, Puerto Rico and Curacao, N.W.I., Jan. 29-Feb. 8, 1956. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York 21, New York, U. S. A., Executive Director.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, EXTRAORDINARY GENERAL ASSEMBLY, Burgenstock, Nidwalden, Switzerland, Sept. 21-23, 1956. Dr. Janet Aitken, 30a Acacia Road, London N.W. 1, England, Secretary.

MIDDLE EAST MEDICAL ASSEMBLY, Campus, American University of Beirut, Beirut, Lebanon, April 7-9, 1956. Dr. Virgil C. Scott, American University of Beirut, Beirut, Lebanon, Chairman.

NATIONAL CONGRESS OF PEDIATRICS, Cuidad Universitaria, Mexico D.F., Mexico, May 1-5, 1956. Dr. Ignacio Avila Cisneros, Calzada de Madereros No. 240, Mexico 18, D.F., Mexico, Coordinator.

NORTH QUEENSLAND MEDICAL CONFERENCE, Cairns, North Queensland, Australia, June 25-30, 1956. Dr. W. R. Hersfall, P. O Box 672, Cairns, N.Q., Australia, Secretary.

PAN-AMERICAN ACADEMY OF GENERAL PRACTICE, San Juan, Puerto Rico and Curacao, N.W.I., Jan. 29-Feb. 8, 1956. Dr. Arturo Martinez, 54 East 72d St., New York 21, New York, U. S. A., Secretary.

PAN AMERICAN CONGRESS ON CANCER CYTOLOGY, Miami, Fla., U. S. A., Jan. 8-12, 1957. Dr. J. Ernest Ayre, 1155 N.W. 14th St., Miami, Fla., U. S. A., General Chairman.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, San Juan, Puerto Rico, April 8-12, 1956. Dr. C. E. Munoz MacCormick, Apartado 9111, Santurce 29, Puerto Rico, Secretary General.

PAN AMERICAN MEDICAL WOMEN'S ALLIANCE, Santiago, Chile, March 6-13, 1956. For information address: Dr. Eva Cutright, 458 Beall Ave., Wooster, Ohio, U. S. A.

WORLD CONGRESS ON FERTILITY AND STERILITY, Naples, Italy, May 18-24, 1956. Dr. Maxwell Roland, 114-20 Queens Boulevard, Forest Hills 75, New York, N. Y., U. S. A., Chairman, Liaison Committee.

WORLD MEDICAL ASSOCIATION, Havana, Cuba, Oct. 9-15, 1956. Dr. Louis H. Bauer, 345 East 46th St., New York 17, New York, U. S. A., Secretary-General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Various Centers. April 24-25 (Part II); June 19-20 (Parts I and II); September 4-5 (Part I). Candidates may file applications at any time but they must be received at least six weeks before the date of the examination for which application is made. New candidates should apply by formal registration; registered candidates may notify the board, indicating desired location, date and candidate number. Ex. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 19-21. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

ARKANSAS:* *Examination.* Little Rock, June 14-15. Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Examination.* Los Angeles, Feb. 27-Mar. 1. Sec., Dr. Louis E. Jones, 1020 N St., Room 436, Sacramento.

CONNECTICUT:* *Examination.* New Haven, March 12-14. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven.

DISTRICT OF COLUMBIA:* *Examination.* Washington, May 14-15. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N.W., Washington.

FLORIDA:* *Examination.* Miami Beach, June 24-26. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GEORGIA: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. Cecil L. Clifton, 111 State Capitol, Atlanta 3.

ILLINOIS: *Examination and Reciprocity.* Chicago, April 3-5, June 19-21 and Oct. 9-11. Supt. of Regis., Mr. Frederic B. Selcke, Capitol Building, Springfield.

INDIANA: *Examination.* Indianapolis, June. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

MAINE: *Examination.* Portland, Mar. 13-14. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 13-15. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., Lansing.

MONTANA: *Examination and Reciprocity.* Helena, April 3. Sec., Dr. S. A. Cooney, 7 West 6th Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June 18-20. Director, Bureau of Examining Boards, Mr. Husted K. Watson, 1009 State Capitol Bldg., Lincoln.

NEW HAMPSHIRE: *Examination and Endorsement.* Concord, March 14-16. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 19-22. Sec., Dr. Patrick H. Corrigan, 28 W. State St., Trenton.

NEW MEXICO:* *Examination and Endorsement.* Santa Fe, May 21-22. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NEW YORK: *Examination.* Albany, Buffalo, Syracuse and New York, Feb. 7-10. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

OHIO: *Examination.* Columbus, June 14-16. *Endorsement.* Columbus, April 3. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA:* *Examination.* Oklahoma City, June 5-6. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 18-20. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Reciprocity.* Salt Lake City, Feb. 21. *Examination.* Salt Lake City, July 11-13. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

WEST VIRGINIA: *Examination.* Charleston, July. *Reciprocity.* Charleston, April 23. Sec., Dr. N. H. Dyer, State Office Bldg. No. 3, Charleston.

WISCONSIN:* *Reciprocity,* Madison, Spring; *Reciprocity and Examination.* Milwaukee, July 10-12. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

WYOMING: *Examination and Endorsement.* Cheyenne, Feb. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

ALASKA:* On application in Anchorage, Fairbanks, Juneau and other towns. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Sec., Dr. John E. Kennedy, Agana.

PUERTO RICO: *Examination.* San Juan, Mar. 6-10. Sec., Dr. Joaquin Mercado Cruz, Box 3271, San Juan.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, May 4-5. Sec., Mr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

CONNECTICUT: *Examination.* New Haven, Feb. 11. Address: State Board of Healing Arts, 258 Bradley St., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 23-24. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave. N.W., Washington 6.

FLORIDA: *Examination.* Miami, June 9. Sec., Mr. M. W. Emmel, Box 340, Gainesville.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Feb. 10-11. Sec., Mrs. Anne Baker, 410 W. Michigan Ave., Lansing 15.

OKLAHOMA: *Examination and Reciprocity.* Oklahoma City, Mar. 30-31. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, March 3; June 2, Sept. 8 and Dec. 1. Dr. Earl M. Pallett, Sec., State Board of Higher Education, Eugene.

RHODE ISLAND: *Examination.* Providence, Feb. 15. Admin. of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

TENNESSEE: *Examination.* Memphis, Mar. 21-22. Sec., Mr. O. W. Hyman, 62 S. Dunlap St., Memphis 3.

TEXAS: *Examination.* Galveston, Dallas, and such other locations as are warranted, April. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination.* Madison, April 7 and Milwaukee, June 2. Final date for filing application is Mar. 30. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

ALASKA: *Examination and Reciprocity.* Anchorage and Juneau, first week of February, April, June, August and November. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

*Basic Science Certificate required.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines and forthcoming network television programs on medical subjects is published each week only for the information of readers of THE JOURNAL. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles and programs reported.*

TELEVISION

Monday, Feb. 6

NBC-TV, 9 p. m. EST. "Medic" offers "If Tomorrow Be Sad," a presentation on multiple sclerosis.

NBC-TV, 11 a. m.-noon EST. "Medical and Health News with Howard Whitman," a segment of the "Home" show, will feature a filmed report on the anatomy of the heart, photographed at Franklin Institute, Philadelphia.

ABC-TV, 9:30 p. m. EST. "Medical Horizons" goes to Northwestern University Medical School, Chicago, for a discussion on rheumatic fever.

MAGAZINES

Town Journal, January, 1956

"How to Head Off a Headache," by Howard LaFay

A report from George Washington University Hospital's headache clinic on types of headaches, their cause, and treatment. The clinic has developed a new headache remedy (containing ergot, caffeine, bellafoline and pentobarbital) that is being marketed under the trade name of Cafergot-PB. According to the article, hospital physicians "report that Cafergot-PB seems to be the most effective drug yet devised for the rapid relief of head pain."

The American Weekly, Jan. 15, 1956

"Do You Approve of Sororities?" by Ann Cutler

The author reports a discussion on the emotional impact of the sorority system at the American Medical Association's Annual Meeting in June, 1955. Dr. Jackson A. Smith, a psychiatrist, "suggested that parents preparing to send their daughter to a college or university would do well to fortify the young student against unhappiness and hurt by having the family physician caution her against building too many dreams of college life."

Saturday Evening Post, Jan. 21, 1956

"Death in Small Doses," by Arthur L. Davis

Food and Drug Administration investigators crack down on the illegal sale of amphetamine sulphate to truck drivers.

The American Weekly, Jan. 22, 1956

"This Is Your Future," by William Engle

"Life expectancy in 1900 was 46 for men, 48 for women. Life expectancy by 1965—if the present trend toward longer life goes on—will rise to 70 years for men, 75 for women," reports Mr. Engle. He gives a brief review on medical prospects for the future, touching on drugs, vaccines, transplanted organs, and improved living conditions.

Reader's Digest, February, 1956

"The Test That Tells How Fast We Live," by J. D. Ratcliff

"The basal metabolism test has become one of the foundation stones of modern medicine. With it and kindred tests, doctors are able to find out how well our body engines are functioning. And if something is amiss, the tests point the way to treatment which can restore us to a normally healthy and useful life." Condensed from an article in *Today's Health.*

"Important Facts About Abortion," by Morton Sontheimer

According to the author, America's abortion problem starts with our laws. "Ethical doctors muddle along through the chaos created by (the laws) and the demands of desperate patients." The article is based on a survey made by the *Woman's Home Companion.*

Parents' Magazine, February, 1956

"How Blue Babies Are Saved," by Emmy Lou Fetta Hawkes

Blue babies didn't have a chance to live and grow up just a few years ago. Now 90% of those whose hearts are successfully operated upon are living largely normal and active lives.

Better Living, February, 1956

"Denied a Child," by Dr. Thomas C. Peightal

A professor of gynecology from New York's College of Physicians and Surgeons answers questions from parents who are unable to have children.

Science Digest, February, 1956

"A 'Penicillin' for Polio?" by Arthur J. Snider

The Chicago Daily News science editor discusses the search for a prophylactic or therapeutic drug for poliomyelitis and calls attention to other unsolved problems in the field.

Woman's Home Companion, February, 1956

"When You Need Help!" by Vivian Cadden

A survey by the magazine on quality of emergency ambulance service showed that "Out of 44 major American cities, not more than 15 have good emergency systems. Among 134 small and middle-sized communities, 47 rate good." In conclusion, the article recommends that readers campaign for a single municipal agency to be responsible for operation of the emergency system.

"You Can Beat a Cold," by Constance Freiss, M.D.

A doctor advises busy housewives that there is no quick, easy cure for the common cold. She warns against making demands for penicillin shots and outlines the necessary home care.

"Get Your Family Well Faster," by Herbert Pollack, M.D.

A nutritionist points out that a wife or mother can hasten convalescence of a sick member of her family by having a clear knowledge of the patient's nutritive needs.

GOVERNMENT SERVICES

NAVY

Medical and Dental Symposium.—A medical and dental symposium for the armed services has been scheduled for March 21-23 on "Developments in Military Medicine and Dentistry with Special Emphasis on Atomic Warfare, Special Weapons, and Isotopes." The meeting on the first day will be conducted at the Naval Hospital, Chelsea, Mass. On the mornings of the second and third days, clinics will be scheduled at hospitals in Boston on the "Treatment of Diseases with Radioactive Isotopes." Afternoon lectures will be given at the Jimmy Fund Foundation Building and in the auditorium at the New England Deaconess Hospital. Programs and additional information may be obtained by addressing the District Medical Office, First Naval District, 495 Summer Street, Boston 10, Mass. This symposium has been approved for retirement point credit for those in attendance who are on the active status list in the armed services reserve programs.

Medical Officers Retired.—The following Navy medical department officers were transferred to the retired list of the Navy on Jan. 1, 1956: nondisability retirements—Capt. Henry G. Bullwinkel, M. C., Capt. Norris M. Hardisty, M. C., and Lieut. Vernon W. Burkett, M. S. C.; physical disability retirements—Capt. John M. Whalen, M. C., and Commander Alvis B. Dickson, M. C.

VETERANS ADMINISTRATION

New Program for Long-Term Mental Patients.—After a three-year test at the VA hospital in Albany, N. Y., the Veterans Administration is expanding a new type of program to other general medical and surgical VA hospitals in an attempt to recondition selected long-term psychiatric patients from closed ward status in neuropsychiatric hospitals to open ward status in general medical and surgical hospitals. The patients selected for the treatment are those who have both mental and physical disabilities and who have shown little change in their mental condition after many years of treatment in neuropsychiatric hospitals. The objective in transferring them to general medical and surgical hospitals is to provide more intensive treatment and rehabilitation for their physical disabilities and, at the same time, to apply "total push" measures in reconditioning them for greater freedom and independence in the hospital and community.

The Albany Hospital reported the following results in three years of working with about 350 chronic schizophrenics, some of whom had been hospitalized in closed wards of NP hospitals for as long as 35 years: 1. All patients live in open wards, in daily contact with nonmental patients. 2. Sixty have progressed to the point where they are working regularly at jobs in the hospital. 3. Fourteen already have made trial visits home with 10 more slated for similar predischarge privileges—a remarkable accomplishment in itself in view of their long hospitalization.

During the study at Albany, Dr. Ian C. Funk, chief of psychiatry, and his chief clinical psychologist, Leo Shatin, Ph.D., kept security measures at a minimum. Wards were opened where possible, and the patients used regular dining room facilities. Recreational areas and activities in the 11-floor building were made available to the mental patients. Employees throughout the hospital came in frequent contact with almost all of the transferred mental patients. The patients also were permitted contact with younger and nonmental patients. The Albany staff next evolved a program of group psychotherapy to supplement and expand the open ward type of treatment. In this program, Dr. Funk had the assistance of Dr. Leonard Rockmore, staff psychiatrist, and Dr. Earl X. Freed, staff psychologist. The success of the "total push" program at Albany is one of the bases for the present expansion to other general medical and surgical hospitals capable of developing the program.

Rehabilitation of Veterans with Circulatory Ailments.—A Veterans Administration follow-up study has disclosed that 95 of every 100 veterans with heart and circulatory ailments rehabilitated through Public Law 16 training are working today as productive wage-earning citizens. They can be found in farms, factories, offices, and laboratories. Eighty-six per cent of the employed veterans are using skills they acquired in this training. Of the veterans not working, half of them said they were unemployed for reasons not related to their hearts or circulatory disabilities. VA's study covered a sampling of the many disabled World War II veterans who received vocational rehabilitation training under Public Law 16, of whom about 40,000 suffered from heart and circulatory disabilities.

The average weekly income of those thus rehabilitated was more than $70 a week. The follow-up study found that veterans with heart and circulatory disabilities aimed for top-level professional and managerial occupations at a higher rate than veterans with other disabilities. On the other hand, those with heart and circulatory ailments tended to veer away from occupations requiring a great deal of physical activity.

Residencies in Psychiatry Available.—The Veterans Administration Hospital, Lyons, N. J., has available residencies in psychiatry for a one to three-year period that are fully accredited by the American Board of Psychiatry and Neurology. The training program consists of lectures, conferences, and seminars under the direction of the department of psychiatry, New York Medical College, and offers intensive training, both intramurally and through rotation in special hospitals and clinics in the adjacent area. There is, in addition, a series of extensive guest lecturers as well as an annual institute at this hospital. Training may commence at any time.

Neurological Residency Available.—A neurological residency has recently been approved at the Veterans Administration Hospital, Oakland, Calif. The appointment is for two years. Applicants must be graduates of class A medical schools and citizens of the United States. Under the career residency program, this position is available at the salary of a full-time staff physician in the Veterans Administration, as well as on the usual Veterans Administration resident salary schedule. For information, write to the Director of Professional Services, VA Hospital, 13th and Harrison streets, Oakland 12, Calif.

Personal.—Dr. James D. Murphy, chief surgical service, at the VA hospital in Oteen, N. C., has been appointed manager of the VA hospital at Baltimore, Md., succeeding Dr. Theodore R. Dayton, who will retire. Dr. Murphy has been in federal service since 1933 and transferred to VA in 1939. In 1943, he was transferred to his present post at Oteen. He was in private practice in Chicago from 1926 to 1933.

PUBLIC HEALTH SERVICE

Dr. Estella Warner Retires.—The Public Health Service announced the retirement of Dr. Estella Ford Warner, chief of the program development branch of the Division of International Health, on Jan. 13th.

Dr. Warner, the first woman ever commissioned in the PHS, became a commissioned officer in 1932. Her first international assignment was in 1951, when she went to Lebanon to help establish a school of public health at the American University of Beirut medical college. Between 1952 and 1955, she was stationed in New Delhi, India, where she assisted the government of India in planning public health technical assistance programs, particularly for rural areas.

Other assignments held by Dr. Warner include: chief of the division of state relations; medical director of the Kansas City regional office; medical consultant of the Chicago regional office; and regional medical director assigned to the U. S. Bureau of Indian Affairs. Prior to entering PHS, Dr. Warner served in state and local health departments in Oregon and was in private practice in Portland. She is leaving Washington to reside in Albuquerque, N. Mex.

DEATHS

Kaiser, Albert David ✱ Rochester, N. Y.; born in Philadelphia Nov. 20, 1887; Harvard Medical School, Boston, 1913; since 1945 professor of child hygiene at the University of Rochester School of Medicine and Dentistry, where he was a member of the board of trustees, and assistant professor of pediatrics from 1925 to 1932, when he became associate professor of pediatrics; trustee of the Colgate Rochester Divinity School; since 1945 health officer of Rochester; specialist certified by the American Board of Pediatrics and the American Board of Public Health; from 1940 to 1943 member of the advisory committee of the Children's Bureau of the Department of Labor in Washington; served as consultant in pediatrics to the state department of health and as a member of the state health preparedness commission; chairman, Section on Pediatrics, American Medical Association 1939-1940; past-president of the Medical Society of the County of Monroe and the Public Health Nursing Association; honorary president of the Tuberculosis and Health Association of Rochester and Monroe County; member of the American Pediatric Society; fellow of the American Academy of Pediatrics and the American Public Health Association; the Rochester Academy of Medicine, of which he was president in 1937, established the Albert David Kaiser award and medal to be presented to a fellow of the academy who made significant contributions to the science of medicine or public health; in 1945 the Rochester Museum Association, of which he was past-president, presented him with a medal for "civic responsiveness, his standing as a physician, his professional interest in public health and his achievements in the fields of exploration, scholarship and leadership"; past-president and board member of the Rochester Museum of Arts and Sciences; past-president of the New York State Public Health Association and the New York State Health Officers Association; served overseas during World War I; trustee of the Rochester Chamber of Commerce; director of the Rochester chapter, American Red Cross; founder and the first executive director of the Rochester Regional Hospital Council, Inc., serving from 1946 to 1951; vice-chairman of the New York State Mental Hygiene Council; since 1947 director of the Eastman Dental Dispensary; consultant in pediatrics at the Rochester General and Genesee hospitals, and attending pediatrician at the Convalescent Hospital for Children and the Monroe County Infirmary; trustee, Trudeau (N. Y.) Sanatorium; assistant pediatrician at the Strong Memorial Hospital, where he died Nov. 1, aged 67, of coronary thrombosis.

Lerrigo, Charles Henry ✱ Topeka, Kan.; born in Birmingham, England, Sept. 12, 1872; Homeopathic Medical College of Missouri, St. Louis, 1900; member of the American Trudeau Society; fellow of the American Public Health Association and the American Geriatrics Association; for 25 years executive secretary, then secretary emeritus, of the Kansas Tuberculosis and Health Association, formerly known as the Kansas Society for the Study and Prevention of Tuberculosis, which he helped organize; for many years a member of the state board of health, of which he was past-president; in 1922 resigned as state registrar in the vital statistics division of the state board of health; in 1947 received the Crumbine medal from the Kansas Public Health Association for his accomplishments and in 1948 was honored at its annual meeting for his outstanding contribution to public health in Kansas; served overseas during World War I; on the staffs of the Christ's and St. Francis hospitals; formerly on the faculty of Washburn College; author of "Better Half of Your Life" and "Doc Williams"; died in Sylacauga, Ala., Dec. 4, aged 83, of carcinoma of the esophagus.

Bothe, Albert Edward ✱ Philadelphia; born in Camden, N. J., Aug. 5, 1891; Long Island College Hospital, Brooklyn, N. Y., 1920; professor of clinical urology at the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; specialist certified by the American Board of Urology; member of the American Urological Association, Eastern Surgical Society, and the American Association for the Advancement of Science; served during World War II; held an honorary degree from the University of Madrid; consultant at Children's Hospital; chief of urology at Fitzgerald-Mercy Hospital in Darby, at Jeanes Hospital, Hospital of the University of Pennsylvania, and the Misericordia Hospital, where he died Nov. 11, aged 64, of cerebral hemorrhage.

Abercrombie, Anna D. Schultze ✱ Lutherville, Md.; Woman's Medical College of Baltimore, 1908; died Oct. 31, aged 83.

Brigham, Charles F. ✱ St. Cloud, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; for many years city physician; died in St. Cloud Hospital Oct. 15, aged 79, of acute coronary disease and carcinoma of the prostate.

Browning, Ernest Ras ✱ Hot Springs National Park, Ark.; University of Arkansas School of Medicine, Little Rock, 1913; past-president of the Garland County Medical Society; on the staffs of St. Joseph's Hospitals; died Oct. 4, aged 73, of a heart attack.

Butler, George Vincent, Rochester, N. Y.; University of Buffalo School of Medicine, 1921; member of the Medical Society of the State of New York and the American College of Radiology; specialist certified by the American Board of Radiology; served as president of the Rochester Roentgen Ray Society; on the staffs of Highland, St. Mary's, and Park Avenue hospitals; died Dec. 10, aged 57, of coronary thrombosis.

Caisse, Georges Emile ✱ Lowell, Mass.; Tufts College Medical School, Boston, 1899; formerly member of the welfare board; died Nov. 2, aged 83, of arteriosclerotic heart disease.

Carden, Floyd Cornelius ✱ Cleveland; Meharry Medical College, Nashville, Tenn., 1930; served with the U. S. Public Health Service during World War II; died Nov. 5, aged 53.

Cohen, Hymen Leon ✱ New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1924; clinical instructor in obstetrics and gynecology at Louisiana State University School of Medicine; at one time on the faculty of his alma mater; on the staffs of the Touro Infirmary, and Charity and Sara Mayo hospitals; died Dec. 3, aged 53, of coronary thrombosis.

Cook, Bryan Jarred, Whitmore Lake, Mich.; Memphis (Tenn.) Hospital Medical College, 1897; served during World War I; died Oct. 11, aged 82, of myocarditis.

Cooper, Burpee ✱ Arcata, Calif.; University of Arkansas School of Medicine, Little Rock, 1912; past-president of the Humboldt County Medical Society; formerly associated with the Indian Service; served on the staffs of the General Hospital in Eureka and the Trinity Hospital; past-president of the Chamber of Commerce; died in Eureka Nov. 7, aged 72, of nephritis.

Cowan, Riley ✱ Van Buren, Ark. (licensed in Arkansas in 1907); past-president and secretary of the Crawford County Medical Society; at one time county health officer; local surgeon for the Missouri Pacific Railroad; died in Fort Smith Oct. 8, aged 79, of injuries received when his car crashed into a truck.

Crume, George P., Minneapolis; University of Louisville (Ky.) Medical Department, 1891; served on the staffs of the Swedish and City hospitals; died Nov. 4, aged 86, of carcinoma of the liver.

Davitt, George Glass ✱ Los Angeles; Yale University School of Medicine, New Haven, Conn., 1913; at one time on the faculty of his alma mater; died Nov. 28, aged 76, of cerebrovascular accident.

Eckfeldt, Thomas Hooper ✱ Peterborough, N. H.; Temple University School of Medicine, Philadelphia, 1950; certified by the National Board of Medical Examiners; vice-president of the medical staff of the Monadnock Community Hospital, where he died Nov. 13, aged 35, of acute coronary occlusion.

✱ Indicates Member of the American Medical Association.

Ericson, Reinhold Milton ✱ Wayzata, Minn.; Washington University School of Medicine, St. Louis, 1928; fellow of the International College of Surgeons and the American College of Surgeons; served during World War II; on the honorary staff of Swedish Hospital in Minneapolis, where he died Nov. 13, aged 53, of coronary thrombosis.

Evans, John Henry, Buffalo; University of Buffalo School of Medicine, 1908; professor of anesthesiology emeritus at his alma mater; specialist certified by the American Board of Anesthesiology; an associate member of the American Medical Association; member of the American Society of Anesthesiologists; past-president of the Associated Anesthetists of the United States and Canada; served on the staffs of the Children's Hospital and Buffalo General Hospital, where he died Nov. 27, aged 79, of coronary thrombosis.

Field, Augustus Marion ✱ Hayward, Calif.; California Medical College, San Francisco, 1896; University of Southern California School of Medicine, Los Angeles, 1903; died Nov. 29, aged 95.

Gilmore, George Harrison, Murray, Neb.; Rush Medical College, Chicago, 1895; served during World War I; died Oct. 9, aged 88, of chronic myocarditis and Parkinson's disease.

Graves, Rex Vale ✱ Fullerton, Calif.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1903; died Dec. 3, aged 77.

Green, William Arthur, Asheville, N. C.; Chicago Homeopathic Medical College, 1901; died Oct. 14, aged 78, of coronary thrombosis, hypertension, and arteriosclerosis.

Grillin, Michael Joseph, Fall River, Mass.; College of Physicians and Surgeons, Baltimore, 1907; died Nov. 13, aged 79, of heart disease.

Haarlammert, Charles Joseph ✱ Cincinnati; Cincinnati College of Medicine and Surgery, 1899; died in the Cincinnati Sanitarium Nov. 30, aged 82, of coronary occlusion and arteriosclerosis.

Harris, Henry T. ✱ Washington, Ga.; University of Georgia Medical Department, Augusta, 1898; died Oct. 19, aged 81, of cerebral thrombosis and arteriosclerosis.

Holst, John Burton, Little Falls, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1895; served as president of the staff of St. Gabriel's Hospital; died in the Fairview Hospital, Minneapolis, Oct. 17, aged 83, of bronchopneumonia.

Kerley, James Hoyt, New York City; Columbia University College of Physicians and Surgeons, New York City, 1914; member of the Medical Society of the State of New York; specialist certified by the American Board of Pediatrics; served during World War I; consultant at Babies and Bellevue hospitals; died in the New York Hospital Nov. 20, aged 68, of cerebral thrombosis following an operation for acoustic neurinoma.

King, Robert, Rochester, N. Y.; McGill University Faculty of Medicine, Montreal, Canada, 1903; served during World War I; formerly pathologist at the Central Islip (N. Y.) State Hospital and the Rochester State Hospital; died in the Rochester General Hospital Dec. 8, aged 83, of cerebral hemorrhage.

Kramer, Aaron Sigmund ✱ Brooklyn, N. Y.; Tulane University of Louisiana School of Medicine, New Orleans, 1930; served overseas during World War II and was awarded a Bronze Star; on the staffs of the Kings County and Israel Zion hospitals; died Nov. 10, aged 50, of rheumatic heart disease.

Larsen, Marven Orville ✱ Middletown, N. Y.; College of Medical Evangelists, Loma Linda and Los Angeles, 1950; certified by the National Board of Medical Examiners; interned at St. Luke's Hospital in Newburgh; formerly a resident at the Wyckoff Heights Hospital in Brooklyn and Fordham Hospital in New York City; died Oct. 21, aged 38, of injuries received in a plane crash.

Laubersheimer, George Ashby, Los Angeles; University of Southern California College of Medicine, Los Angeles, 1900; an associate member of the American Medical Association; died Nov. 13, aged 78, of carcinoma with metastases to the bones and liver.

Levine, Sinclair Simcha, Hartford, Conn.; College of Physicians and Surgeons, Baltimore, 1912; member of the Connecticut State Medical Society; also a pharmacist; consulting physician for the Connecticut Bureau of Vocational Rehabilitation; on the courtesy staffs of the St. Francis Hospital and Mount Sinai Hospital, where he died Nov. 14, aged 72, of salmonella bacteremia and cerebral hemorrhage.

Lewis, Morley Brown ✱ Sag Harbor, N. Y.; Baltimore Medical College, 1896; served as mayor; a founder of the Southampton (N. Y.) Hospital, where he was an honorary staff member, and where he died Dec. 3, aged 86, of lymphatic leukemia.

Lewkowicz, Ferdinand Frederick ✱ Tannersville, N. Y.; Uniwersytet Jagiellónski Wydzial Lekarski, Cracow, Poland, 1934; at one time a captain in the Polish Army; on the staff of the Memorial Hospital of Greene County in Catskill; died Oct. 24, aged 46, of injuries received in an automobile accident.

Lyle, William Gordon, New York City; College of Physicians and Surgeons, medical department of Columbia College, New York City, 1892; an associate member of the American Medical Association; on the staffs of the Roosevelt and St. Luke's hospitals; died Nov. 25, aged 84, of cerebral hemorrhage.

McDonald, Joseph John Alexander ✱ New York City; University of Toronto Faculty of Medicine, Toronto, Canada, 1923; medical director of the Borden Company for the United States and Canada; served with the Royal Canadian Air Force during World War I; member of the staffs of the Flower and Fifth Avenue and St. Clare's hospitals; died in the French Hospital Nov. 6, aged 60.

Miller, George Henry ✱ Bellaire, Mich.; Rush Medical College, Chicago, 1897; emeritus member of the Illinois State Medical Society; served overseas during World War I; for many years worked for the board of health in Chicago, where he was an emeritus member of the staff of the Norwegian American Hospital; died Nov. 13, aged 79, of diabetes mellitus and arteriosclerosis.

Motamed, Hossein ✱ Garden City, N. Y.; Madresseh Teb, Teheran, Persia, 1915; died Sept. 23, aged 62, of coronary thrombosis.

Potoszky, Henry ✱ Columbia, S. C.; University and Bellevue Hospital Medical College, New York City, 1933; specialist certified by the American Board of Radiology; member of the American College of Radiology; served during World War II; chief of the department of radiology, Veterans Administration Hospital; died Oct. 23, aged 46.

Pyles, Richard Henry, Glendale, Calif.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1902; veteran of the Spanish-American War and World War I; served on the staff of the Orthopaedic Hospital; died Dec. 1, aged 77.

Sandsteed, Harold Russell ✱ Medical Director, U. S. Public Health Service, Silver Springs, Md.; University of Nebraska College of Medicine, 1931; medical director of the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health in Bethesda, and executive director, interdepartmental committee on nutrition for National Defense, National Institutes of Health; formerly assistant professor of medicine, Vanderbilt University School of Medicine in Nashville, Tenn.; died in Longmont, Colo., Nov. 1, aged 50, in an airplane crash.

Westmoreland, James Paschal ✱ Houston, Texas; Hospital College of Medicine, Louisville, Ky., 1907; for many years on the staff of St. Joseph's Infirmary; died Oct. 22, aged 75, of heart disease.

Wolfe, Howard Hartnette ✱ San Francisco; University of Minnesota Medical School, Minneapolis, 1922; served during World Wars I and II; chief medical officer of the San Francisco regional office of the Veterans Administration; died in the Veterans Administration Hospital, Fort Miley, Nov. 8, aged 55, of cancer.

Wollner, Henry, New York City; New York University Medical College, New York City, 1896; for many years associated with St. Joseph's Hospital, where he died Nov. 9, aged 85.

FOREIGN LETTERS

AUSTRIA

Pulmonary Hemorrhage and Mitral Stenosis.—At the meeting of the Society of Internal Medicine of Vienna on Oct. 27, Dr. N. Stefenelli presented the case of a man, aged 44, who died of pulmonary hemorrhage associated with mitral stenosis. The hemorrhage originated in ectatic bronchial veins, which led to partial obstruction of the air passage and finally to asphyxia. It appears that dilatation of the bronchial veins in patients with mitral stenosis is caused by the formation of a collateral circulation stimulated by increased pressure in the pulmonary veins. The collateral passages are formed by way of bronchial veins in the region of the vena azygos and vena hemiazygos. Cicatricial changes of the bronchial mucosa seemed to favor the development of hemorrhages.

Posthepatitic Hyperbilirubinemia.—At the same meeting Dr. H. Kalk reported on a series of 159 patients with posthepatitic hyperbilirubinemia. This disorder takes the form of a mild jaundice after successive attacks of hepatitis with gastrointestinal symptoms in an indirect hyperbilirubinemia. It chiefly attacks men who give the impression of being neurasthenic and hypochondriacal. The sedimentation rate is extremely slow. The titration values in Gross's test are high, whereas other tests of the liver function give normal results. Only the bilirubin tolerance test shows decided retention of biliary pigment. In about one-third of the patients, signs of a mild hemolysis are demonstrable. Liver biopsy specimens disclose no signs of inflammation, but there is activation of Kupffer's cells and accumulations of a brown pigment. Efforts were made to differentiate this brown pigment in the hepatogram. It is probably a masked iron compound. Posthepatitic hyperbilirubinemia seems to be related to congenital hemolytic jaundice. The prognosis of the disease is favorable. Restriction or prohibition of meat in the diet is important in the treatment. The following factors contribute to the cause of this disorder: (1) an increase in the rate of hemolysis; (2) insufficient excretion of bilirubin; and (3) disturbed hemosynthesis with temporary accumulation of porphyrin, a part of which is converted into bilirubin. The symptoms of posthepatitic hyperbilirubinemia are probably caused by the third factor. The speaker suggested that, in some patients to whom the collective terms "neurasthenia-hypochondria" and "sympathetic dystonia" are applied, disturbances in the porphyrin metabolism may exist.

BRAZIL

Spontaneous Pneumothorax.—In spite of the progress of chemotherapy, antibiotics, and surgical collapse, pneumoperitoneum still has a definite place in the treatment of pulmonary tuberculosis. One of the advantages of pneumoperitoneum is the infrequency of accidents and complications in the course of its maintenance. When spontaneous pneumothorax follows pneumoperitoneum, it must be caused by abdominal air if it is to be considered a complication of the pneumoperitoneum. Spontaneous pneumothorax may occur during the therapeutic procedure without being caused by it. Dr. Newton Bethlem and co-workers in *Revista brasileira de tuberculose* (23:61, 1955) reported on a patient in whom spontaneous pneumothorax, as a complication, occurred three times. The spontaneous formation of pneumothorax, with the air transferred from the abdomen, was evidenced each time by roentgenograms showing the disappearance of the abdominal air. The passage of the air from the abdomen to the thorax is brought about by two different mechanisms. The air may pass through the diaphragmatic hiatuses of the esophagus and great vessels, producing an emphysema of the mediastinum, rupturing the pleura and causing a spontaneous pneumothorax, as a rule on the left side, or the air may pass through perforations of the diaphragm caused by inflammatory, degenerative, congenital, or accidental processes. The authors believed that in their patient, in whom the pneumothorax each time occurred on the right side, a diaphragmatic defect and the dynamic action of the pneumoperitoneum pushing the liver and the diaphragm in opposite directions caused the pneumothorax by increasing the tension in the right hemidiaphragm. They believe that, when spontaneous pneumothorax occurs, the use of pneumoperitoneum should be abandoned. Although in their case they discontinued pneumoperitoneum only after the third occurrence of the pneumothorax, they do not consider this to be the best procedure.

Angiographic Diagnosis of Subdural Hematoma.—The Prize Enjolras Vampré of the Associação Paulista de Medicina was conferred on Drs. José Zaclis and R. A. Tenuto for their studies on the angiographic diagnosis of subdural hematoma. In their series of eight patients, six had unilateral hematomas, diagnosed by means of cerebral angiography. In only one the elliptical, nonvascular area, which is pathognomonic of subdural hematomas, could be seen, under frontal projection in the arterial phase. In the other patients the diagnosis of subdural hematoma would not have been made if the venous phase had not been considered. The arterial displacement seen in most patients with subdural hematoma is of no diagnostic value, because such a displacement may occur in any space-occupying lesion. Besides, a subdural hematoma may occur with no arterial dislocation, especially in patients with bilateral subdural collections of blood. On the other hand, a single, unilateral hematoma with no shifting of the anterior cerebral artery to the opposite side may also occur. In the last three cases of this series, there was no significant displacement of the anterior cerebral artery: the venous phase and further surgical exploration showed the hematomas to be bilateral in two. In the third of these patients the anterior cerebral artery had a normal course, in spite of the space taken by a single hematoma. Thus, if the venous phase shows the characteristic avascular area of subdural hematoma with no displacement in the arterial phase, it does not necessarily mean that the hematoma is bilateral. Nevertheless, angiograms of the opposite side must always be made. Since, in angiographic diagnosis of subdural hematoma, the accuracy of the venous phase in sagittal projection seems to be proved, Zaclis and Tenuto believe that the above-mentioned step should be taken even if, in order to achieve it, a new injection of contrast medium is required.

Double Uterus with Rudimentary Vagina.—Dr. Elsa A. Puretz described in *Anais brasileiros de ginecologia* (40:1, 1955) a rare case of malformation of the female genitalia in which several internal and external anomalies occurred simultaneously—a solid rudimentary double uterus with rudimentary vagina. Only four similar cases have been described. The patient was a married woman of 21 years, who came to the outpatient department of the Institute of Gynecology because she had never menstruated and because sexual intercourse was always painful. Since the age of 17 years she had observed a cyclic syndrome of two or three days' duration repeated at about a three to four-week interval, consisting of lower abdominal heaviness, pricking pains in the right iliac fossa, mastalgia, and headache. The physical examination showed marked tenderness over McBurney's point. The urethra was widened and retroflexed, resembling hypospadias. The vagina was reduced to a small cul-de-sac admitting only the terminal phalanx of the index finger. The double-touch examination revealed the absence of uterus and cervix. A diagnosis of appendicitis and agenesia of the uterus was made. An exploratory laparotomy and appendectomy were performed, and two rudimentary, solid round-shaped uteri of soft consistency were found, the right one measuring about 2.5 cm. and the left one about 1.5 cm. in diameter. They were bound by a peritoneal band. At the right side there was a normal oviduct, but the left one was rudimentary. The ovaries were

The items in these letters are contributed by regular correspondents in the various foreign countries.

polycystic and enlarged to about twice their normal size. A week later, a neoelytroplasty was performed by the Wharton technique, and after a month the vagina, showing a good epithelization, admitted the full length of the index finger.

Neurological Symptoms of Polycythemia Vera.—Drs. Roberto Melaragno Jr. and J. A. Levy reported on (*Arq. neuro-psiquiat.* 13:313, 1955) a series of eight patients with polycythemia vera. All had symptoms and/or signs attributable to lesions of the nervous system. In five the symptoms were subjective (headache, dizziness, and asthenia). In only one was there a history of a transient left hemiparesis. In three of the five patients the authors observed a marked, retinal venous congestion; in another the eyegrounds were normal; and in one no ophthalmoscopic examination was made. In the three remaining patients, besides identical subjective symptoms, there were neurological signs. In one there were signs of occlusion of the left middle cerebral artery, in one there was a sensory-motor paraplegia, and one manifested a medullary tegmental paralysis (Babinski-Nageotte syndrome), indicating the occlusion of the left posteroinferior cerebral artery. The authors believe that the neurological phenomena occurring with polycythemia vera must be explained by various factors, especially such as the following: (1) the increased blood viscosity that increases the cerebrovascular resistance, (2) the lessening of the flow and speed of the blood in the brain, and (3) the arteriosclerosis, the development of which seems to be favored by polycythemic conditions.

Duplay's Disease.—According to Dr. Nelson Carvalho (*Rev. Hosp. clin.* 10:187, 1955) the best name for Duplay's disease (subdeltoid or subacromial bursitis) would be "calcifying peritendonitis," because the symptoms originate from the tendons, in particular those of the supraspinatus muscle. The disease is characterized by pain and limitation of movement of the shoulder joint, which may be severe. The principal cause of the disease seems to be the occlusion of the vessels of the tendon from hypertrophy of the tunica media, which is followed by local necrosis. As a result of the deficient oxidation, the tissues become devitalized and calcific deposits are formed. Irradiation causes vasodilatation, hyperemia, and absorption of the calcium deposits, thereby relieving the pain and restoring mobility. Refractory cases (about 20%) require operation.

Escherichia Coli Infection.—At a recent meeting of the Associação Paulista de Medicina, Dr. A. E. Taunay and his coworkers reported that pathogenic types of Escherichia coli were isolated from the stools and nasopharyngeal secretions of newborn infants. Of 55 such infants with diarrhea, 13 had Esch. coli, type O 111-B 4, in their stools. One also had Salmonella sp. (type butantan). Of a control group of 10 breast-fed and 10 bottle-fed newborn infants considered normal, 4 showed slight diarrhea. Of these, three had Esch. coli, type O 111-B 4, in their stools. Two infants had Esch. coli, type 26-B 6, in their nasopharyngeal secretions but not in their stools. No pathogenic Esch. coli was isolated from the feces and nasopharyngeal secretions of the nurses attending the infants or from the milk fed to the infants.

ENGLAND

Society of Gastroenterologists.—At the annual meeting of the British Society of Gastroenterologists in Oxford in November, Dr. Edith Bülbring (Oxford) described her work on ionic and electropotential variations at the cell membrane of smooth muscles. Using microelectrodes, she found a steady potential difference across smooth muscle membranes of –40 to –80 millivolts. During activity the membrane becomes permeable to potassium ions, which move out while sodium ions move in, causing a fall in potential. In the recovery phase the potassium ions move back. Histamine and acetylcholine produce contractions of intestinal muscle after nerve block, so that the ionic movements and potential differences are inherent properties of the cell. Epinephrine causes relaxation and might permit restoration of the ionic gradient across the cell membrane. Professor Burn said that the intestine becomes atonic after reduction in the serum level of sodium chloride and that the serum potassium then rises. Possibly potassium ions replace sodium so that the gradient between intracellular and extracellular ions is increased. Peristalsis is markedly slowed by morphine, less by methadone, and least by meperidine. Sir Howard Florey (Oxford) said that, to show where gastric mucus is actively secreted, he had given radioactive sodium sulfate to animals before cutting sections of gastric and duodenal mucosa. Goblet cells and, in some species, neck cell glands show radioactivity, but Brunner's glands and surface epithelial cells do not, showing that they do not secrete mucus. He did not think mucus acted as a chemical buffer but it might act mechanically. Dr. B. C. Morson (London) found that in 200 gastrectomies metaplasia was present in 65% of the specimens from patients with duodenal ulcer, in 82% of those with gastric ulcer, and in 92% of those with neoplasm. He noted that, in patients with pernicious anemia, metaplasia was extensive in the fundus and body of the stomach.

An analysis by Dr. G. Watkinson (Leeds) of 12,641 autopsies suggested a correlation between sclerosis of the coronary artery and peptic ulcer. The effects of corticotropin were discussed by Drs. J. Kyle and R. B. Welbourn (Belfast), who said that it had no effect on the gastric function of normal animals, but that hypophysectomy diminished the volume and acidity of gastric juice and this could be restored by administering cortisone or corticotropin. Prof. J. G. Goligher, condemned the Billroth 1 operation for duodenal ulcer, the recurrence rate following which he found to be 15%, compared with 1.5% for the Polya operation. Mr. Capper (Bristol) commented on the frequency of bilious regurgitation after high resection and gastroduodenal anastomosis, compared with its low incidence after a more conservative resection and similar anastomosis. According to Dr. R. Schneider (Birmingham), fat absorption occurred in the absence of emulsification, bile, and pancreatic lipase, although these were essential for optimal absorption. He also showed that the intestinal mucosa produced its own lipase. Olive oil in a fine emulsion passed into the lacteals without the aid of upper intestinal juices, as did oleic acid, but not sodium oleate.

Dr. G. N. Chandler (Leeds) said that he administered to rats olive oil labeled with radioactive iodine and found with the aid of a Geiger counter that the uptake of fat was greatest in the third quarter of the intestine. Even if this part of the intestine were transplanted nearer the duodenum it still functioned in the same way, and Dr. Chandler therefore concluded that the epithelial cells in this part of the intestine had a specific fat-absorbing capacity. Dr. P. Snow (Manchester) commented on the effect of alcohol, which brought on pain and flushing of the face and upper part of the chest in patients with Hodgkin's disease. He thought that this might be due to the vasodilator effect of serotonin (5-hydroxytryptamine), which is present in abnormal quantities in the blood of some patients with malignant carcinoids.

Cholesterol, Diet, and Coronary Disease.—More and more attention is being paid to the epidemiology of coronary artery disease, which is showing an increase in all industrialized countries. The role of dietary fat as a factor in its causation is further emphasized by the work of Professor Keys, of Minnesota, in collaboration with Professor Brock and his group at the University of Cape Town (*Lancet* 2:1103, 1955). They studied the bodily characteristics, serum cholesterol and serum lipoprotein levels, diet, and personal habits of 383 men aged 40-58 residing in the Cape Peninsula and representative of three racial groups—Bantu, Cape Negro, and European. These groups differ strikingly in the incidence of coronary heart disease, which is rare in the Bantu, commoner in the Cape Negro, and most common in those of European descent. Highly significant differences in the mean total serum cholesterol, and particularly in the cholesterol level in the beta-lipoprotein fraction of the serum, were found when the men were classified according to their racial origin. The Bantus had the lowest levels, the Europeans the highest, and the Cape Negroes were in between. There were also large differences found in the fat consumption of these racial groups, that of the Europeans being more than twice that of the Bantu, with the Cape Negroes intermediate. Further subdivision within these three racial groups on the basis of income revealed that with an increase in income from subgroup to subgroup two consistent and parallel trends emerged—an increase of mean total serum cholesterol, particularly the beta-lipoprotein fraction, and an in-

crease in the consumption of animal fat. At any given income level, the mean levels of total cholesterol and beta-lipoprotein cholesterol were much the same for the three races. The results of the survey support the view that the dietary intake of fat influences the level of the serum cholesterol, particularly that in the beta-lipoproteins, and in turn may be one of the major factors influencing the pathogenesis of coronary heart disease. The impressions of Keys and Brock on the relative incidence of myocardial infarction in these three racial groups has been confirmed by Drs. Vogelpoel and Schrive of the University of Cape Town. From the examination of 5,000 electrocardiograms, they concluded that myocardial infarction was uncommon in the Bantu (0.9% of cases examined), more often found in the Cape Negroes (6.8%) and commonest in the Europeans (13.54%).

Cancer and Bronchitis.—During an attempt to find out if mustard gas, which is carcinogenic to animals, is carcinogenic to man, Case and Lea have discovered a possible association between cancer and bronchitis (*Brit. J. Prev. & Social Med.* 9:62, 1955). They studied the records of a number of pensioners of World War I to see if those who had suffered from mustard gas poisoning had a high incidence of cancer of the lung and in other sites. The incidence of cancer in those exposed to mustard gas was no greater than in those that had not been exposed, but the authors found that deaths due to cancer of the lung among 1,421 World War I pensioners who were known to have bronchitis at the time they were pensioned were twice the rate of the general population. The number of deaths from cancer in other sites among the war pensioners followed the pattern seen in men of the same age in the general population. A possible explanation is that cancer of the lung may be associated with the inflammation and degeneration of long-standing bronchitis or that bronchitis, like lung cancer, is in part caused by long-continued smoking. Bronchitis is commoner among smokers than among nonsmokers, and the incidence of disease increases with the amount smoked. The figures do not definitely prove a causative association between bronchitis and lung cancer. Several sources of error in Case and Lea's data are possible. The cause of death is not always given correctly in death certificates unless an autopsy is performed. A chronic history of chest disease might influence the diagnosis of the cause of death. The presence of long-standing chest disease might also cause a more thorough examination of the chest to be made and a malignant condition that might otherwise be missed to be discovered. In the authors' opinion the various possibilities of bias in their figures would result in cancer of the lung being under rather than overdiagnosed.

Prescribers' Notes.—The Ministry of Health regularly issues a bulletin, *Prescribers' Notes*, and sends it to physicians working under the National Health Service. The object of this bulletin is to persuade them not to prescribe useless drugs or expensive drugs if there is a cheaper equivalent. In the last issue, clinical work is described as showing that vitamin B_{12} and liver extract have no tonic effect in patients with normal, or nearly normal, blood findings. Beneficial results were obtained with injections of vitamin B_{12}, liver extract, and a placebo in 49, 48, and 43%, respectively, of patients given these substances as tonics. The abusive use of expensive orally given penicillin preparations is also discussed. According to the bulletin, ordinary sodium penicillin gives peak blood levels quicker than benzathine penicillin G, and its absorption is just as reliable. The much higher cost of the latter is pointed out. A comparison is also made of the efficacy of tetracycline and penicillin in the treatment of lobar pneumonia. Tetracycline is not superior to penicillin and has a greater tendency to produce side-effects, besides being far more expensive. Physicians are also urged to read the Drug Tariff, an official list of drug prices and titles, and not to order expensive drugs, such as antibiotics, in round numbers but to calculate as exactly as possible the number of tablets or capsules likely to be required by the patient. An up-to-date booklet was recently sent to physicians giving the actual cost to the National Health Service of many standard preparations included in the National Formulary or the British Pharmacopoeia Codex and the comparative costs of equivalent or similar proprietary preparations side by side. In *Prescribers' Notes*, physicians are requested to read, study, and digest these lists and not to prescribe drugs advertised to the public or those not of proved therapeutic value.

Banning of Heroin.—Following the banning by government decree of the manufacture and therefore prescription of heroin in Great Britain, which was effective Jan. 1, several London hospitals nullified the effect of the prohibition by previously laying in large stocks. One hospital that uses over 20,000 doses a year has laid in a seven-year supply. Twelve hospitals have made a last-minute appeal to the Minister of Health, asking him to withdraw his assent to the imposing of the ban by the Home Secretary. In effect, the Minister has said that he consulted his experts and that they approved of the ban. Some physicians believe that no heroin substitute exists that will effectively relieve patients with metastatic neoplasms of the bone, severe burns, and pain due to arterial disease and alleviate coughs due to pulmonary neoplasms and tracheitis. It is not so much the banning of heroin that worries some of them, but the dictatorial method by which it has been done. They claim that the Minister of Health does not get opinions representative of the medical profession as a whole. It is said that the documents and the issues coming before his medical advisers are too often confidential. As there are only 52 known heroin addicts, or one in a million persons, many physicians wonder why heroin is to be banned. They consider that prohibition of its export would protect other countries from receiving it. It is also believed that the government's decision on heroin touches a fundamental principle and confirms the fear that physicians have had since they were "nationalized." If a physician thinks that heroin is necessary for his patient, what right has a minister or a government to stand between him and his patient?

Unlawful Injection.—A boy of 17 was awarded $633 damages at Norwich County Court because a physician gave him an injection against his will. He claimed damages for assault, negligence, and breach of duty and sued the local hospital regional board, as well as the physician who gave the injection. The boy took his younger brother to a chest clinic, where he had been summoned because tuberculosis had been detected in the family and it was considered advisable to do a Mantoux test. The physician and nurse at the clinic thought that the older boy should be tested as well. He refused but ultimately and reluctantly gave his consent when told that his parents had agreed when called by telephone. The judge said that the physician and nurse were acting in the best interests of the boy, but no one could be forced to submit to such a procedure against his will. Actually the parents had not given their consent, and the judge said that the boy had been tricked into having the Mantoux test done. The damages were assessed at more than a pinprick because the boy developed psoriasis after the event. Two physicians said that psoriasis could result from the test, and two others disagreed. The judge assessed damages for assault at $73.50, and, for the psoriasis, which he held was caused by the Mantoux test, he awarded $560.

Doctor at Large.—Richard Gordon, a pseudonym hiding the identity of an Oxford anesthesiologist and former assistant editor of the *British Medical Journal*, has produced yet another humorous novel of medical life. After qualifying, the hero of the book thinks that the path of progress in his profession is strewn with roses. He soon realizes that life is a struggle and, when he takes the position of junior assistant casualty officer in St. Swithin's Hospital, he makes a number of mistakes that come to the notice of the professor of surgery. He then seeks work at a medical employment agency and gathers experience the hard way. He goes to an industrial practice in the Midlands, where his colleague's amorous and neglected wife is an even greater worry than the patients. Then he graduates to London's West End, where he impresses his patients with a Rolls Royce car and numerous diagnostic gadgets. Tiring of ministering to the wealthy, he goes into country practice and finally returns to St. Swithin's as a senior surgeon, where he eventually achieves matrimony. As in his other books, Dr. Gordon has a lot of fun at the expense of the medical profession, although not in an unkindly or cynical way. No doubt this book will be filmed as were *Doctor in the House* and *Doctor at Sea*.

Mysterious Illness at a School.—Sixty of 190 children in a school at Tottington, Lancashire, suffered from a mysterious illness, the cause of which was not apparent. The divisional medical officer, who investigated it, stated that the symptoms suggested poisoning of the nervous system by a toxic agent. Two of the children became unconscious and several semiconscious. Vomiting, dilatation of the pupils, and changes in the pulse rate were also noted. Pyrexia was absent. The children recovered in a few days. Food poisoning and carbon monoxide poisoning were at first suspected but eliminated as causes. Fumes from an organic phosphorus insecticide may have been liberated from sacks used for cleaning. These were stored in a cellar near a central heating plant and could have given off toxic fumes when the plant warmed up.

Dentifrice and Dental Decay.—The British Dental Association in a recent statement denies that the use of any type of dentifrice will cure or prevent dental decay. This statement was thought necessary in view of the number of incorrect advertising claims that certain dentifrices protect teeth against decay. The association favors brushing to clean the teeth and points out that cleaning is all that a dentifrice can do.

PERU

Balantidiasis.—In Peru intestinal parasitism is an important public health problem. Balantidiasis is found in almost all parts of the country, according to Dr. Hugo Lumbreras Cruz of the Dos de Mayo Hospital in an address before the second Peruvian Congress of Medicine in Lima in October. This disease has an insidious onset and runs a prolonged course. After studying 29 patients with balantidial colitis, Dr. Lumbreras Cruz concludes that this infection, when symptomatic, may appear as balantidial dysentery, in which secondary infection by enteric bacteria plays an important role, or the more typical simple balantidial diarrhea in which patients have occasional bouts of acute dysentery, especially after dietary indiscretions. An asymptomatic form exists in healthy carriers who may, however, suffer from time to time with slight, undefined gastric and intestinal disturbances. Ulcers of the colon resembling those observed in amebiasis are always present in balantidiasis, regardless of the clinical findings. Evidence that Balantidium coli possesses a histolytic action was presented. Iron-deficiency anemia and an elevated sedimentation rate are the most constant laboratory findings. Eosinophilia is seen but rarely. Hypoproteinemia was observed in about 50% of the speaker's patients. Ulcers of the colon are not always found on proctoscopic examination, and, in every case, the diagnosis must be confirmed by finding the parasites in the stools. Oxytetracycline, the drug of choice in therapy of balantidiasis, was given to patients in Dr. Lumbreras Cruz's series and to 10 others for four to nine days in an average daily dose of 1 gm. After the second day of therapy, parasitological, as well as clinical, improvement was evident in most of the patients. The stools were completely free of parasites within five days in all patients. Transient meteorism was observed in a few patients. No recurrences were observed, but the follow-up period was not long enough to assure that definitive cure had been achieved. Supportive and symptomatic therapy are also important, and chlortetracycline has been found to be effective.

Trypanosomiasis.— At the same meeting Dr. Lumbreras Cruz reported that trypanosomiasis is common in Peru but is often overlooked or wrongly diagnosed. Surveys in some endemic regions revealed that as many as 34% of the insect vectors were infested. Using serodiagnostic methods, the speaker found that the 20% of human beings living in houses that contained infested vectors harbored the parasites. He urged physicians to give more attention to the recognition and control of this disease.

Uropepsin.—Determination of urinary pepsinogen excretion should be added to the routine laboratory tests, according to Dr. Alberto Guzmán Barrón of the National University of San Marcos in an address before the National Convention of Pathology in September. The administration of 25 mg. of corticotropin to normal subjects nearly doubles the excretion of uropepsin, but patients with pernicious anemia, who have no detectable pepsinogen in urine, do not respond to administration of corticotropin and even cortisone does not cause the enzyme to appear in the urine. Patients with other types of anemia show responses similar to those observed in normal subjects. In the presence of adrenal cortical hypofunction, the corticotropin does not increase the urinary pepsinogen excretion; however, cortisone does, and, due to the simplicity of this test, the speaker recommended its use in diagnosis of incipient hypoadrenocorticism. He has found in 20 patients with peptic ulcer that the average daily excretion of urinary pepsinogen was above normal, but he doubts that the assay of uropepsin is sufficiently reliable to replace gastric analysis in the diagnosis of peptic ulcer. Patients with a partial gastrectomy showed a diminished daily excretion of urinary pepsinogen, and uropepsin was totally absent in five patients who had undergone total gastrectomy. Four patients with primary hepatic carcinoma showed a urinary pepsinogen level lower than normal. The only clinical or radiological sign of gastric disturbance exhibited by these patients was an asymptomatic achlorhydria. Similar levels of uropepsin were detected in five patients with gastric cancer. The average normal daily urinary pepsinogen excretion was 29 units in men and 19 units in women.

Effect of Carbon Dioxide on the Respiratory Center.—Prof. Alberto Hurtado of the Institute de Biología Andina has found that the respiratory center at high altitudes acquires an increased sensibility to carbon dioxide regardless of the degree of blood oxygenation. He reported the results of his investigations at the National Congress of Medicine in October. He undertook his study to determine why subjects living at high altitude show, as an adaptative process to the low pressure of oxygen in the inspired air, an increase of the ventilatory function. He gave mixtures of carbon dioxide, air, and oxygen to natives living at Morococha, a place 14,900 ft. (4.5 km.) above sea level (barometric pressure, 445 mm. Hg); then, he measured the ventilatory response and simultaneously estimated the pO_2 and pCO_2 in the alveolar air. Similar comparative studies were performed in subjects living permanently at sea level. The ventilatory response was much greater in those living at high altitudes than in those living at sea level, and this obtains even though oxygen is given with carbon dioxide.

SWEDEN

Fight Against Poliomyelitis.—At the World Health Organization conference in Stockholm in November, it was reported that results from five countries in which the Salk vaccine was being used showed a good degree of protection in the age group in which it was used. It was considered that when properly manufactured and tested the Salk vaccine was as safe as any vaccine used against other diseases. The general view was that the potentially dangerous Mahoney strain of type 1 virus used in the Salk vaccine should preferably be replaced by a safer strain. According to Dr. Albert Sabin a strain could be produced as antigenically effective as the Mahoney strain without any of its risks. It was recommended that, in countries with a high incidence of poliomyelitis, mass vaccination against the disease should be done routinely. In countries with a low incidence of the paralytic form of the disease, the decision whether to vaccinate or not should be taken only after careful consideration of all relevant circumstances. About 10 million children in five countries have been vaccinated without any undesirable effects, except in the few cases in the United States caused by faulty vaccine. Permanent control of all vaccines produced is still needed. In Canada, where 860,000 children 5 to 9 years of age were vaccinated, there was a paralysis rate of 1.07 per 100,000 vaccinated, against 5.39 per 100,000 unvaccinated. In Denmark, no case of poliomyelitis has been reported among 425,000 children vaccinated in April, 1955, but there have been only seven cases in the whole population since then. The Salk vaccine appears to protect children 6 to 10 years of age, the only age group for which proofs are sufficiently clear to allow a conclusive statement to be made. It is impossible to say how long the immunity will last. The seriousness of the poliomyelitis problem should be balanced against the costs and practical possibilities of carrying out mass vaccination. As some countries have more knowledge of the disease and vaccination than others, they should pool their knowledge for the common good. Among

the questions considered was that of the possibility of inoculations, especially those causing strong local reactions, increasing the risk of infection with poliomyelitis. Such a risk was admitted. Tests with live vaccine are still in an early stage of development, and research on them should be encouraged.

SWITZERLAND

Swiss Society of Gastroenterology.—Professor Kalk of Kassel, Germany, reported on liver function tests and liver biopsy to the annual meeting of the Swiss Society of Gastroenterology at Basel in November. Judging from the results of 2,500 biopsies, Professor Kalk believes that there is no strict correlation between the function tests and the histological data. Often the function tests reveal no disturbance, while the biopsy specimen shows a definitely pathological state. The opposite case is rare. With reservation, one can say that the bilirubin levels and the sulfobromophthalein show disorder soonest, when it is a question of a pure diffuse cellular lesion. The tests of serologic lability that are based on protein shifts, especially on an increase of gamma globulins, do not show pathological states until mesenchymal reactions have set in, that is, reactions of the reticuloendothelial system. As soon as the activity of the inflammatory processes in the mesenchyma diminishes, the lability tests gradually return to normal. Gross's reaction is the best indication of the state of these processes. The sedimentation rate is also an index of the inflammatory states. This research points up the limitations of our present hepatic tests and the importance of biopsies in the diagnosis of liver disease.

S. Scheidegger and H. J. Fahrlaender of Basel said that chlorpromazine may produce an intrahepatic block. The protein reactions are usually negative, but the alkaline phosphatase is increased by this drug. In some of the patients receiving chlorpromazine therapy, liver biopsy shows the presence of biliary thrombosis, fatty degeneration, and round-cell infiltration. The speakers studied several fatal cases and found severe well-delineated toxic changes, with advanced dissociation, fatty degeneration, and inflammatory infiltration. These disorders are comparable to those appearing after the administration of cinchophen or the sulfonamides. It seems that they are of an allergic character.

W. Hess of Basel analyzed the risks of abdominal operations in elderly patients, on the basis of 536 such operations performed on persons 60 to 93 years old. Although there were no deaths from the repair of simple hernias and uncomplicated appendectomies, the mortality from strangulated hernia and perforated appendixes was great. Simple gastric resection had a mortality rate of 5.1%, partial gastrectomy for cancer 5.7%, total gastrectomy 6.8%, colonic resection 4.8%, and operations on the rectum 18.6%. The decrease in the operative risk in recent years has encouraged more active therapy of abdominal diseases in the aged.

H. Baur of Basel studied the clinical significance of urocathepsin determination, an excellent guide to the daily activity of the stomach. The activity of this ferment is optimal at the physiological pH of the stomach. Cathepsin continues the proteolysis in the neutral milieu of the small intestine. Urocathepsin determination is a complement to gastric-tube determination for hydrochloric acid and pepsin. It is the basis of replacement therapy with preparations of digestive ferments with cathepsic activity. It is also a complement to other tubeless tests such as the determination of gastric acidity by quinine-resin exchange.

P. Decker and F. Saegesser of Lausanne are not enthusiastic about the long-term results of surgical extirpation of cancer of the esophagus and cardia. The palliative results are often remarkable, however, and it is a mistake to evaluate the results only by the number of five-year survivals. Surgical treatment of these cancers is completely justified.

F. Deucher of Zurich defended antethoracic esophagoplasty, done in a one-stage operation of about four hours. After wound healing, the cancer is irradiated. This symptomatic therapy is at least as useful to the patient as a vain attempt at radical surgery. Gastrostomy or jejunostomy should be used only after an attempt at antethoracic esophagoplasty has failed.

M. Demole of Geneva studied the incidence of ulcerative colitis from 1946 to 1950 in 41 Swiss hospitals and found it to be 0.6 per 1,000. At the time of hospitalization the disease had lasted on an average of five years in men and three and a half years in women. More than a third of the patients were seen during the first bout of the disease, which is particularly severe, since its mortality rate is 40% as compared with a rate of 18% from a relapse. Many patients get well after a first bout, but only 10% leave the hospital in a stabilized condition. The total mortality rate from the disease is 25%. Half of those operated on die despite surgical treatment.

World Health Organization Meeting on Cardiovascular Disease.—A study group of the World Health Organization on atherosclerosis, which met at Geneva, recommended that an international research project into the cause and prevention of heart disease be undertaken. At present the only advice given to patients is moderation in all things, particularly food, alcohol, and tobacco. Ischemic heart disease, which is a public health problem, should receive special attention as there is no clear evidence of any one causative factor at work. Probably a number of factors operate, their action differing according to the ethnic group and social status of the patient. In the United States, Great Britain, and Sweden many more men than women die from ischemic heart disease between the ages of 40 and 60, whereas in the Netherlands there are more deaths from this cause among women than among men. Deaths from all forms of heart disease at all ages per 100,000 persons were 569 for men and 430 for women in the United States; 567 for men and 568 for women in Great Britain; and 301 for men and 307 for women in the Netherlands. Diet may play a part in some countries. There are, however, populations with a far greater incidence of obesity than in the United States or Great Britain, but with a much lower incidence of ischemic heart disease. Calculations based on insurance statistics show that if all the overweight persons in the United States were eliminated from the records, the death rate from this form of heart disease would still be greater than in Italy and the Scandinavian countries, even though obesity is common in these countries. Populations on low-fat diets have a low incidence of atherosclerosis and ischemic heart disease, and during the war the reduction in fat intake in Norway was followed by a reduction in the death rate from coronary thrombosis. The study group recognizes physical inactivity as a factor. Professional and business men suffer from ischemic heart disease more frequently than those in occupations necessitating more physical exercise. Hypertension may or may not be associated with cardiac damage. The relationship between heavy tobacco consumption and cardiovascular disease is now obvious. Alcoholism may play a part as statistics from various countries show that bartenders are especially prone to cardiovascular and renal disease.

Cancer Predisposition.—Schinz and Reich of the University of Zurich published a work based on statistics of deaths from cancer in Switzerland in 1952. All persons are exposed to carcinogenic substances, the action of which manifests itself after the subject has absorbed a significant quantity. The quantity of carcinogens absorbed rather than the age of the patient determines whether the disease will develop. The critical amount varies from person to person according to an asymmetrical Gauss curve, either because the subjects react differently to the same dose or because of variations in the total dose. The authors established curves for different age groups, showing the frequency of deaths from carcinoma as compared with 100,000 living persons of each age group. The mortality is low in young persons, but it rises rapidly after a certain age. These curves show peculiarities of different localizations of cancer. Since 1901, deaths from pulmonary cancer in men have shown yearly peaks, i. e., diminutions in mortality after a maximum occurring between the ages of 60 and 69 years. The general mortality from cancer has, however, been decreasing since the beginning of the century in younger men and increasing in the older ones, thus tending to erase the peak of the first curve. These data must be interpreted in the light of the fact that formerly the diagnosis often went unrecognized, especially in older persons. Thus, the authors' theory is not that of predisposition according to age but of exposition according to age.

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CORRESPONDENCE

CHEST X-RAY SURVEYS

To the Editor:—In an editorial in THE JOURNAL, April 23, 1955, page 1499, Garland indicated that the yield of new active cases of tuberculosis resulting from chest x-ray surveys was small. He raised the question whether it would not be timely and appropriate to reevaluate the usefulness of this measure as a case-finding tool. During the past two years an intensive chest x-ray survey program has been pursued in Seattle and King County, Washington. During 1954, two mobile units took 80,431 miniature films. In addition, a stationary unit was placed in the city jail for the purpose of obtaining a film on every new inmate. During 1954, 10,970 films were obtained from this group. Also health card x-rays for all food handlers are mandatory, and the number of films taken during the past year was 15,459. From the mobile units that took over 80,000 films, 76 active cases of tuberculosis were discovered (0.94 active cases per 1,000 films). From the 10,970 films taken in the city jail, 82 patients had proved active cases of tuberculosis, making an astounding yield of 7.5 cases per 1,000 films. Of the approximately 15,000 food-handler films, 23 demonstrated active disease (1.5 per 1,000 films). During the past two years 20 counties in Washington (outside of King County) have participated in fast tempo community-wide chest x-ray surveys. During 1954, the number of films obtained from this source was 202,669, or 71.2% of the x-rayable population, which is designated to indicate persons 15 years of age or over. Final reports concerning the yield from this source have not as yet been returned because of the short follow-up period. Interim reports indicate that thus far one active case has been identified per 2,000 films taken, representing a cost of $805 per case. It appeared to us that, if chest x-ray surveys are of the dubious value that Garland indicated, then such a conclusion should be readily apparent from a survey of admissions to a tuberculosis hospital. Accordingly, beginning May 11, 1955, 150 consecutive new admissions to Firland Sanatorium with active, pulmonary tuberculosis were studied. This required a period of about five months, the final patient being surveyed on Oct. 10, 1955. These patients were studied particularly with regard to the source of admission (individual or agency responsible for the detection of the patient's tuberculosis), the extent of disease, and the presence of cavity.

150 Consecutive New Admissions of Patients with Pulmonary Tuberculosis, May 11-Oct. 10, 1955

Source of X-Ray	No. of Cases	Extent of Disease			No. of Cases		
		Minimal	Moderately Advanced	Far Advanced	With Cavity	Per Cent	With Bilateral Cavity
Mobile unit, jail, or health card	85	42	41	2	12	14	1
Private physician or private hospital	47	6	22	19	29	62	5
County General Hospital	18	1	7	10	13	72	5
Total	150	49	70	31	54		

The table indicates that well over 50% of these cases were identified by means of some survey unit, with 31% being detected by private physicians and private hospitals and 12% discovered by the County General Hospital. Furthermore, of the total of 49 minimal cases, 42 were discovered by survey units and only 7 by private physicians or the County General Hospital. Conversely, of the 31 cases of far-advanced tuberculosis, 29 were detected as a result of examinations by private physicians and the County General Hospital, with only 2 cases of far-advanced disease emanating from the survey units. It is extremely significant that 13 of the 18 cases detected by the County General Hospital exhibited cavity (72%), and in 5 of these cases cavities were present bilaterally. This is in marked contrast to the cases discovered by survey units, where only 12 out of 85 cases (14%) revealed excavation; only one instance of bilateral cavity occurred in this latter group. Further analysis of this table indicates that a patient who had his disease detected by a survey unit had about a 50% chance of exhibiting only minimal disease. In the cases detected by a private physician, there was a 40% chance of the disease being far advanced in extent and greater than 60% chance that his disease would be cavitary in nature. Continuing in this vein, in cases discovered at the County General Hospital, the patients had a greater than 50% chance of their disease being far advanced, and, furthermore, there was a 72% likelihood that their disease would be cavitary in nature. It seems reasonable to assume that if such extensive facilities for x-ray surveys had not existed in Seattle, King County, and the state of Washington, many of the patients whose disease was detected by these methods would have continued their usual life in their normal environment and would have served as reservoirs of infection until their symptoms had reached such a clamorous stage as to make them seek advice from a private physician or from the County General Hospital. Obviously, at this later date, their disease would have been more extensive and more difficult to treat than it would have been had a survey film been performed earlier.

Garland emphasizes that efficient antituberculosis antibiotics are now at hand, and, therefore, with the yield from surveys being relatively low, the question of the value of surveys should be reopened. In our experience, by far the great majority of treatment failures (and they still do occur despite our potent antituberculosis agents) are seen in patients who are admitted with far-advanced cavitary tuberculosis. In other words, from the patient's point of view and the hospital's point of view, chest x-ray surveys deliver tuberculous patients to the hospital in an eminently treatable condition. Present emphasis should not be placed on the discontinuance of case-finding measures, such as fast tempo chest x-ray surveys, routine jail x-rays, food-handler x-rays, and routine x-rays of general hospital admissions but on the continuing and intensive education of the private physician, so that he may play a more effective part in the detection of this disease. Similarly, the adoption of the policy of routine x-rays on all admissions to general hospitals, both private and public, most certainly would lead not only to the identification of a greater number of cases of tuberculosis but also to the detection of this disease in its earlier stages. Before this study was completed the policy of routine x-rays of all admissions was adopted by the County General Hospital. It appears clear then that the private physician, the general hospital, and the locally sponsored x-ray surveys all have an important and complementary part to play in the detection of this disease. Should each of these segments of the medical community perform their role with proper diligence, they would automatically add immeasurably to the patient's chances of reaching the tuberculosis hospital with the type and extent of disease that can be treated successfully in a relatively short period of time. The time has not yet arrived to abandon survey techniques. Greater emphasis should be placed on the education of the private physician to expand his role in the detection of tuberculosis and on the in-

doctrination of the public to seek and accept the case-finding measures employed in the private physician's office and in general hospitals.

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MEDICAL STATISTICS

To the Editor:—In an article on the use of dramamine to control postoperative vomiting, in THE JOURNAL, Dec. 3, 1955, page 1342, the authors state that their statisticians at the University of Washington analyzed their results by the chi-square test and found p less than 1 in 100 million. From this, they say, the statisticians concluded that "the probability was less than one in a hundred million that the drug did not significantly reduce the incidence of postoperative vomiting." This conclusion is the result of a misleading and widespread error in the interpretation of medical statistics. What the test showed in this case is that, "On the assumption that the drug does not affect the incidence of postoperative vomiting, the probability is less than one in a hundred million that chi-square would have turned out as large as it did." But this is far different from the conclusion that was drawn. The nonmathematician will see this better by the following illustration: The probability that, with well-shuffled cards and an honest deal, a given player will get 13 cards of a suit is only 1 in 158,753,389,900. But, if a player does in fact get a 13-card suit on a deal, this by no means shows that the chance is only 1 in 158 billion plus that the deal was honest; that is, it does not show that the probability is 158,753,389,899 out of 158,753,389,900 that the deal was crooked.

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MISCELLANY

FREAK ACCIDENTS

Paul Jones, Chicago

The following odd little happenings and many others were uncovered by the National Safety Council in its annual roundup of freak accidents. Here's the rundown on the dizzy doings in 1955:

Gene Scott, of Rushville, Neb., had hoped his hunting trip would turn up something special. It did. He was getting out of his car when a gust of wind blew the door shut on his coat pocket. A rifle shell in his pocket shot him. In New Liberty, Iowa, 12-year-old David Dahl placed his rifle against a ladder in the barn and started to climb to the loft. His dog jumped on the ladder, struck the rifle trigger with his paw, and shot his ascending master just below the hayloft. Some fish stories are greeted by raised eyebrows, but when Bobby Bright, of Gonzales, Texas, reported that he had been shot by a fish, no one could doubt him. He had the fish, the gun, and the wound to prove it. A freshly caught catfish flopped around in the bottom of Bobby's boat, struck the trigger of his rifle and shot him in the arm. In Detroit Mrs. Dorothy Gazzeny brushed her teeth so vigorously she swallowed the toothbrush. Fortunately, she had another.

At least two dogs tried their paw at driving an automobile in 1955—a Doberman pinscher in Fort Wayne, Ind., and a boxer in Black River Falls, Wis. Both ended up by crashing into something. They also ended up in the doghouse. Timothy Davis made headlines in Long Beach, Calif., by taking his grandfather for a little spin in the family car. The trip was newsworthy for three reasons. One was that the car tore off the porch of a nearby house and came so near running down a neighbor that she fainted. The second was that Timothy propelled the car by sitting on the accelerator. The third was that Timmy was only 2 years old. Timmy's mother had left him in the car with his grandfather. Timmy turned on the ignition, sat on the gas pedal, and—swoosh! Now, if a 2-year-old boy can drive a car by sitting on the accelerator, a 2-year-old girl can do it too—and do it better. So Margaret Ann Kilby, of Indianapolis, did it. Margaret Ann wasn't content to crash into a mere house. She rammed into a fireplug, knocked out the neighborhood water supply for three hours, turned the street into a sheet of ice, and wrecked the car. Another woman driver, eh, fellas?

The Dew Drop Inn at Port Huron, Mich., lived up to its name during a wild wind and rain storm, and dropped into Anchor Bay. One brink too many! Traffic experts say it's safe to go on the green light. Try to tell that to E. T. Drake Jr., of Atlanta, Ga. As he dutifully obeyed an overhead traffic light that flashed him a green go-ahead signal, the light fell on top of his car and sent him to the hospital. Drake saw red. The sign over the door of a used car salesroom in Los Angeles said, "We need your car—drive in!" Lewis Jackson Jr. did—with his throttle stuck. The car crashed through a heavy wooden door, sideswiped two glistening cars on the showroom floor, ran head-on into a costly convertible, and bounced the convertible into another car. They took down the sign. Stanton Sapp and his brother Daniel happened to run into each other on the street in their home town, Mount Vernon, Ohio. That would have been perfectly all right if each of the brothers hadn't been driving a car. Neither was injured in the head-on crash, but it did prove the need for the safety slogan, "Be Your Brother's Keeper—Stop Accidents!"

Every theatrical act strives for a knockout finish. The ballet "Streetcar Named Desire" literally achieved it. As tiny ballerina Nora Kaye whirled in the middle of a pirouette during a New York performance, her elbow caught her husky partner Igor Youskevitch smack in the face, and he went down for the count. Ordinarily, a hung jury is one that fails to agree. But the jury that hung midway between the first and second floors of the courthouse in Reading, Pa., in a stalled elevator for almost an hour agreed perfectly. It wanted down. Four-year-old Walter Adams Jr. was showing his younger brother some of the acrobatic stunts he had seen on TV, when he happened to glance out the window of his fourth-floor apartment in New York City. He noticed that several small girls on the sidewalk 40 ft. below were observing his antics. Walter decided to show them something really good. He opened the window, put his hands together like a high diver, and took off. The girls pulled him out of a big snowbank and carried him up, crying, to his mother. Nothing was hurt but his pride.

On the same day in June, 1955, two planes were brought down in the United States—not by antiaircraft fire, but by a steer and a jackrabbit. The steer was being chased through a wheat field near Bremen, Ind., by a low-flying plane whose pilot, Bob Unsicker, dived again and again at the animal in an attempt to guide it toward a gate. Suddenly it leaped up and was hit by the plane's wheel. The plane went out of control and crashed into a treetop. The pilot escaped with minor injuries. The jackrabbit scored its hit near Grand Forks, N. D. It did it by the simple act of leaping high into the air directly in the path of a crop-dusting plane being flown close to the ground by Leo Mondry. A damaged propeller forced the plane to land. In Hollywood, Calif., where even toys must be colossal or bigger,

Director of Public Information, National Safety Council.

the Burns and Allen television show was using a 20 lb. stuffed Teddy bear in a department store scene. The king-sized bear fell off the shelf, bopped Gracie Allen on the head and knocked her out cold.

Walter Bergman, of Ashton, Idaho, was aware that his jalopy had served him long and well, but he didn't realize how faithful it was until he parked it in front of the postoffice and hurried in to get his mail. Somehow the car slipped into gear and followed him in, right through the postoffice window. In Los Angeles there's a man who just can't stay out of accidents. He's had several traffic escapades that made news for the papers, and this year he fell through the floor of the laboratory where he works and landed 9 ft. below with a bang that knocked him out. His name? No kidding, folks, it's Safety First!

Still think everything happens to you? Monotonous life you lead, isn't it?

LAW DEPARTMENT

MEDICOLEGAL ABSTRACT

Naturopathy as Practice of Medicine.—The defendant was convicted of a violation of the Medical Practice Act, and he appealed to the Court of Appeals of Maryland.

The act provides that it shall be unlawful to practice medicine without first having obtained a license from the board of medical examiners and without having filed such license with the clerk of the circuit court in the county in which the practice is intended. The defendant had neither been licensed by the board nor had he filed the required license with the county clerk. He had filed, however, a certificate from a board of naturopathic examiners certifying that he was qualified to practice as a naturopathic physician.

The defendant admitted that he had been practicing medicine, but he contended that the legislature never intended to include the practice of naturopathy within the scope of the Medical Practice Act and that, under the common law, naturopaths have the right to practice their profession. The Court admitted that, at common law, the practice of medicine was open to all who wished to engage in it but pointed out that the right to practice medicine is subject to the police power of the state to protect and preserve the public health through regulation of that practice and those engaged therein. The statute defines a practitioner of medicine as any person who, for compensation, ". . . shall operate on, profess to heal, prescribe for, or otherwise treat any physical or mental ailment or supposed mental ailment of another, or who shall . . . undertake by any appliance, operation or treatment of whatever nature, to cure, heal or treat any bodily or mental ailment or supposed ailment of another; or who . . . shall undertake to treat, heal, cure, drive away or remove any physical or mental ailment, or supposed ailment of another, by mental or other process, exercised or invoked on the part of either the healer or the patient or both . . ." Although there are certain exceptions to this broad definition of practicing medicine, naturopathy is not one of such exceptions. In the Court's opinion it was absolutely clear from the language of the statute that the legislature intended "practice of medicine" to include not only the application of medicine to patients but also any practice of the art of healing disease and preserving health other than the special branches expressly excepted. The certificate of the board of naturopathic examiners, which the defendant filed with the clerk, the Court pointed out, did not authorize him to treat disease, because that board was created by the Maryland Naturopathic Association, not by the legislature.

The defendant contended that, since the legislature had expressly provided for the licensing of special branches of the healing art, such as osteopathy and chiropody, but had made no provision for licensing naturopaths, it should therefore be inferred that naturopaths may practice without a license. The Court pointed out that, while bills have been introduced in the legislature to permit and regulate the practice of naturopathy, the very fact that no such legislation has been passed indicates instead that the legislature has not thus far intended to permit naturopaths to practice without a license.

In view of the legislature's broad definition of the practice of medicine, from which naturopaths are not excepted, the Court of Appeals concluded that a naturopath is not permitted to engage in the healing art without a license from the board of medical examiners. The Court therefore affirmed the defendant's conviction. *Aitchison v. State, 105 A. (2d) 495 (Md., 1954).*

BUSINESS PRACTICE

SIZE OF A MEDICAL UNIT

A rough estimate of size requirements should be made, plus allowances for other items, in choosing a building site. Off-street parking is perhaps the most important other item; as time goes on, off-street parking may be required of establishments serving the public as well as necessary to good patient relations. When you have decided on the space or site that is large enough for your scale of operations, you should consider whether it will be large enough 10 years from now. Medical units have a tendency to grow and expand, and what may be ample now may be overcrowded and cramped in a few years.

When choosing a building site, topography is often important. The ideal site would be one with a gentle slope providing drainage and one with a commanding position for the building affording a full view of it from the street or highway. Flat sites are easy to deal with, having only the problem of surface drainage. Steeply sloping sites are usually a problem but often lend themselves to a satisfactory and inexpensive solution. Their original cost is often lower, and, when, with a modest amount of grading, the lower part can be filled with dirt from the higher part, the total cost is reasonable. Sometimes a high site on one side of a street can provide dirt to fill a lower one on the other side of the street, giving two usable lots. Do not pass up the more difficult site in a prime location without getting competent advice on how it can be adapted to your needs.

When building or when buying a building, the final consideration is the cost. The actual price of the lot is small in proportion to the final cost of the facility or the actual value of the site, depending on the preceding considerations. Do not be influenced too much or too soon by a low price. Give yourself time to find out all about the site and to determine how it will affect the success of your unit. Although you may not have a great deal of money to invest, you cannot afford to pick a site that will hamper the eventual development of your practice. It is advisable to secure the consultation services of an architect to assist you in the inspection and final determination of suitable property, whether it is to be improved with a new building, with a remodeled one, or with a rented portion of a leased one.

If you have chosen a site on which to build, arrangements should be made to purchase it. If you have decided to renovate an existing building, either rental or long-term lease is acceptable, depending upon the extent of such renovation. If the remodeling is extensive, you need a long-term lease to make it pay. If changes are minor, a monthly rental may serve your purpose.

When you are ready to build or remodel, it is prudent to retain an architect, preferably one experienced in medical buildings. If you are building or remodeling on your own lot, supply the architect with a survey of the site obtained through the services of a civil engineer, showing all the utilities, local conditions, and topography. In any event, provide him with a description of your general requirements and your thinking as to what you want and where you want it. The next step is one of determining the shape and placement of the building or rebuilding to best fit the climate, to provide parking space as well as access and egress for patients, and to get the most out of the structure itself.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Esophagitis, Hiatus Hernia, and Cardiospasm. D. P. Boyd. A. M. A. Arch. Int. Med. 96:724-730 (Dec.) 1955 [Chicago].

Esophagitis is present in only a small minority of the more than 500 patients with hiatal hernia and cardiospasm who are seen at the Lahey Clinic annually. This report is corcerned with only those cases complicated by esophagitis. This is a serious complication, and, inasmuch as several factors may be involved, each patient must be treated on an individual basis and followed for a long period of time. Of the nearly 100 patients with various forms of esophagitis studied at the Lahey Clinic, some had only inflammation, usually in the lower esophagus; some had, in addition, the sliding type of diaphragmatic hiatal hernia; some, the condition that is called cardiospasm; and some patients had had resections of the cardia and lower esophagus for benign or malignant lesions. For the simple lesions that represent the majority, medical measures alone or medical measures combined with periodic dilatation are sufficient to maintain the patient in comfort and good nutrition. Many patients can be taught to perform the dilatations themselves on a weekly or biweekly basis. Medical measures with periodic dilatations likewise may suffice for patients with esophagitis and cardiospasm, or even for those with early fibrous stricture. Patients with diaphragmatic hernia and marked esophagitis with regurgitation are greatly improved by repair of the hernia. Patients with megaesophagus should be treated first by the Heller operation, which gives symptomatic relief. Although the improvement in the megaesophagus may be only slight, a good functional result may be expected. In the past, far-advanced chronic stricture that cannot be dilated has proved to be an exceedingly difficult surgical problem. The author feels that, in many of these patients who are malnourished and anemic and who show general debility, a preliminary gastrostomy or jejunostomy should be carried out and a period of three months or more allowed to elapse before radical surgery is contemplated. The presence of a gastrostomy does complicate the definitive surgical procedure, but the improvement in the patient's condition makes up for any possible disadvantage. In the beginning the author employed conservative resections of the lower esophagus and cardia for this condition but found that esophagitis recurred. This was equally true of the patients who had a megaesophagus. In addition to recurrence of symptoms and secondary stricture, there are two other hazards. One is the development of the so-called vagotomy effect at the pylorus; the second is hemorrhage from the residual esophagus. Now it is the policy of the author to prevent these complications by two specific steps. First, a sufficiently radical resection of the esophagus should be performed. In addition, a pyloroplasty or gastroenterostomy should be done to permit proper emptying of the stomach and to prevent regurgitation.

Diagnostic Methods in an Influenza Vaccine Trial. J. C. McDonald and B. E. Andrews. Brit. M. J. 2:1232-1235 (Nov. 19) 1955 [London, England].

A small-scale influenza vaccine trial was carried out in the Vauxhall Motor Works, Luton, England, with the purpose of determining the practicability of a trial method using both clinical and laboratory tests in the diagnosis of influenza. Of 455 workers employed with the firm who volunteered for the inoculation, 226 received a virus vaccine containing equal proportions of threefold concentrations of the F.M.1 strain and the egg-adapted Liverpool (1951) strain of influenza virus A, adsorbed on aluminum phosphate, and 229 who served as controls were given a low-potency bacterial vaccine of the anticatarrhal type. The inoculated persons were followed up for 12 weeks, and those who were absent from work were visited by one of the authors. Acute respiratory illness was the cause of the absence from work in 82. A clinical diagnosis of influenza was made in 36 of these, and paired serums and throat washings were obtained from them and from 27 additional persons with cold or sore throat. Of the 36 patients, 15 had received the trial vaccine and 21 the control vaccine, absence rates being 6.6% of 226 who received the virus vaccine and 9.2% of 229 who received the control vaccine. Serologic evidence of influenza virus A infection was found in 4 of 226 persons in the trial group and in 16 of 229 persons in the control group, rates of 1.8% and 7% respectively. These results suggest that the assessment of a vaccine on purely clinical grounds might understate the degree of protection provided by the vaccine, whereas one based on serologic findings might exaggerate it. Until it is shown that serologic methods are able to detect cases of influenza equally well in persons who have received an influenza vaccine and in those who have not, serum diagnosis should not be the only method of diagnosis used in a vaccine field trial. In a clinical assessment the fullest use should be made of laboratory evidence to define the epidemic period in the communities concerned and to estimate the proportion of illness in the control group caused by influenza virus infection. This information would enable dilution of the figures by noninfluenzal illness to be reduced and should allow a more accurate assessment of the vaccine to be made.

Studies of Antibodies to Strains of Influenza Virus in Persons of Different Ages in Sera Collected in a Postepidemic Period. A. V. Hennessy, F. M. Davenport and T. Francis Jr. J. Immunol. 75: 401-409 (Nov.) 1955 [Baltimore].

Previous studies had demonstrated that, when antibody levels were measured with many strains of influenza virus in pools of human serums collected from consecutive ages, distinctive patterns of antibody content appeared. The occurrence of an epidemic of influenza A-prime, during 1953 in the United States, afforded an opportunity to extend the studies. Serums were collected by the Serological Laboratory of the University of Michigan Hospital. Preepidemic serums were collected in the fall of 1952, and postepidemic serums were obtained in the late spring, summer, and early fall of 1953. Comparison of antibody content of preepidemic and postepidemic collections of serums pooled by ages showed an increase in the average antibody level of the population in the postepidemic period. Increase in antibody was most marked in the childhood age range when it was measured with recent A-prime isolates. This correlates with the known high incidence of influenza in childhood. Reinforcement of antibody to older strains, i. e., PR8 and swine virus, was demonstrated in adults. These results were in accordance with the concept that the initial infections of childhood orient the antibody-forming mechanism, so that experience later in life to antigenically similar strains confers progressive reinforcement of the primary antibody, which then characterizes that part of the population throughout life. The findings taken in conjunction with an analysis of antibody content of individual serums collected from consecutive age groups in a postepidemic period demonstrated that with experience not only is the antibody mechanism oriented by the initial infections of childhood, but that, with experience, antibody reacting with successively prevalent strains is added. This results in a continuing broadening of the antibody spectrum with age, which confers the immunity on the older age groups in the population. The analysis of the antibody

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levels of individual serums showed that a few individuals in childhood and adolescence also have antibody against major antigens of viruses that are no longer prevalent. This indicates that strains with major antigens of older viruses have had a limited circulation in recent years.

Antibody Responses and Clinical Reactions with Saline and Oil Adjuvant Influenza Virus Vaccines: Second Progress Report by the Medical Research Council's Committee on Clinical Trials of Influenza Vaccine. C. H. Stuart-Harris, C. H. Andrewes, B. E. Andrews and others. Brit. M. J. 2:1229-1232 (Nov. 19) 1955 [London, England].

A trial of approximately one year's duration was carried out to compare the antibody responses and clinical reactions to three virus A influenza vaccines, the strain A/Eng/1/51 being used as the antigen in each case. Two of the vaccines from mouse-adapted and egg-adapted viruses, respectively, were suspended as a water-in-oil emulsion, and the third vaccine from a mouse-adapted-virus was suspended in sodium chloride solution to which aluminum phosphate had been added. Inoculations of the vaccines were carried out on 399 volunteers who were students at 11 British universities that served as volunteer centers. The emulsified vaccines gave a greater and more sustained antibody response than the vaccine suspended in sodium chloride solution, despite the fact that they contained only one-tenth of the amount of virus antigen. A decrease in the antibody levels, observed one year after the inoculation, occurred in all vaccinated groups. No indication of an increased breadth in antibody response to a heterologous virus strain in those given oily vaccines was shown by a small series of tests. The local reactions were more numerous in those who had been given the vaccine suspended in sodium chloride solution than in those who had been given the oily vaccines, but with the latter vaccines unusually extensive and persistent local reactions occurred in two volunteers.

Early Diagnosis of Subacute Bacterial Endocarditis. J. Wedgwood. Lancet 2:1058-1063 (Nov. 19) 1955 [London, England].

The diagnosis of subacute bacterial endocarditis in its early stages is difficult. The author emphasizes the clinical features that may be of value in the recognition of early cases on the basis of 65 cases of subacute bacterial endocarditis admitted to hospital during the 19 years from 1936 to 1954. In every case either the diagnosis was confirmed post mortem or positive blood cultures were obtained in life. Twenty-four patients, admitted since 1949, had been under the author's personal observation. Thirty patients had been treated with adequate courses of penicillin or other antibiotics, and two-thirds of these were alive at the time of writing. The average duration of symptoms, before admission to hospital, was 10 weeks (range 1 to 31 weeks). Most of the patients had received medical attention from an early stage of their illness. A history of either heart disease or rheumatic fever was obtained in 35 of the 65 patients, and dental extraction preceded the onset in 11 patients. Association of the endocarditis with pregnancy was found in 4 of the 12 women of childbearing age. In about four-fifths of the cases the course of the illness was characterized by remissions and exacerbations. A wide variety of diagnoses may be made in subacute bacterial endocarditis. Sometimes the symptoms are serious enough to cause admission to hospital, but often they are thought to be due to relatively minor conditions such as "flu," "gastric flu," fibrositis, sinusitis, anemia, pyelitis, and "nervous breakdown." Subacute bacterial endocarditis will be detected in its early stages only if its possibility is borne in mind. In the cases reviewed a heart murmur was present in 97% and pyrexia in 92% during the first week after admission. Many other diseases may be associated with persistent pyrexia or ill health, but the cases in which subacute bacterial endocarditis is likely can usually be distinguished from the remainder by the presence of a heart murmur.

Chlorpromazine in the Management of Tetanus. A. C. E. Cole and D. H. H. Robertson. Lancet 2:1063-1064 (Nov. 19) 1955 [London, England].

Chlorpromazine hydrochloride (Largactil) is believed to be an antagonist to some central convulsant drugs and to potentiate the action of hypnotics. Because of these two actions the authors administered it, in combination with phenobarbital (phenobarbitone) sodium or chloral hydrate, in six cases of tetanus. Chlorpromazine was administered in doses of 50 mg. intramuscularly (diluted to 10 ml.) or intravenously (diluted to 20 ml.). After such a dose the tetanic spasm was dramatically relieved; the abdominal and back muscles were moderately or completely relaxed; convulsive seizures were inhibited; and a lazy sleepiness replaced the anxious tension of the disease. This effect was prolonged for up to 12 hours by simultaneous injection of 3 grains of phenobarbital sodium. Chlorpromazine, 25 mg. or 10 mg. by mouth, had a less dramatic effect but proved useful in weaning the recovering patients from the injections. The histories of three of the six patients are presented. One of these three cases was fatal. The number of cases treated with chlorpromazine is insufficient to show whether chlorpromazine reduces the mortality from the disease. It does spare the patients much of the acute mental anxiety, physical pain, and exhaustion due to the spasms, and the regimen does not make inordinate demands on the medical and nursing staff.

Splenectomy in the Treatment of Lupus Erythematosus: A Familial Case. P. L. Cardozo. Nederl. tijdschr. geneesk. 99: 3271-3273 (Oct. 29) 1955 (In Dutch) [Haarlem, Netherlands].

The author presents the case of a 16-year-old girl who gave a history of fatigue and periodic rheumatic pains and fever and whose urine contained a trace of albumin. Later the albuminuria increased; the L. E. phenomenon became positive in blood and bone marrow; and the lymph nodes and the spleen became enlarged. When the severity of the disorder increased greatly within a comparatively short time and a connection with hypersplenism seemed evident, a splenectomy was carried out. During the year following the splenectomy the clinical course improved to such an extent that administration of cortisone was no longer necessary. The albuminuria, which ranged between 0.3 and 0.5%, decreased to 0.1%. Two sisters of this patient had died with lupus erythematosus. In these two the disease had become rapidly more severe some months before death, the course having been similar to that in the girl reported previous to splenectomy. Neither of the two sisters had been subjected to splenectomy. The author raises the question whether splenectomy might not be advisable in patients with rheumatoid arthritis who have a positive L. E. test, changes in the peripheral blood, and an enlarged spleen.

Megaloblastic Anemia Following Partial Gastrectomy and Gastro-Enterostomy. J. Badenoch, J. R. Evans, W. C. D. Richards and L. J. Witts. Brit. J. Haemat. 1:339-344 (Oct.) 1955 [Oxford, England].

Although megaloblastic anemia due to deficiency in vitamin B_{12} is almost inevitable after total gastrectomy if the patient survives the operation for six years or longer, it is rare after operations in which a portion of the stomach remains. Recently the authors observed five patients in whom megaloblastic anemia developed after partial gastrectomy and one patient in whom it developed after gastroenterostomy. Since intrinsic factor is secreted by the body of the stomach, it seemed unlikely that the megaloblastic anemia following partial gastrectomy could be due to lack of this factor. However, new techniques of investigation made it possible to study such anemias more fully. All the patients had a macrocytic anemia with megaloblasts in the sternal marrow. They were treated with vitamin B_{12} and four showed optimal response. A fifth showed clinical improvement, but, although the bone marrow changed from megaloblastic to normoblastic erythropoiesis, there was no significant alteration in the peripheral blood; a course of folic acid was ineffective but treatment of the accompanying iron deficiency resulted in a good response. The sixth patient, whose anemia was mild, showed no therapeutic response to either vitamin B_{12} or folic acid. The interval between operation and the diagnosis of megaloblastic anemia ranged from 2 to 17 years. In all instances the total duration of dyspepsia before and after operation had been 20 years or longer. The authors investigated the excretion of acid and uropepsin, and the absorption and excretion of fat. They also attempted to obtain biopsy specimens from the remaining portion of the stomach and estimated the vitamin

B_{12} content of the serum and the secretion of intrinsic factor. The results of the studies indicated that in five of the subjects the anemia was caused by vitamin B_{12} deficiency. There was failure to absorb vitamin B_{12}, which was corrected by the addition of intrinsic factor, and biopsy studies revealed atrophy of the gastric-body mucosa comparable in severity to that seen in pernicious anemia. In the sixth patient the nature of the deficiency and its pathogenesis remained obscure. Steatorrhea was not a significant factor in any of the cases. Since megaloblastic anemia is rare after partial gastrectomy and gastroenterostomy, it seemed possible that the patients might have Addisonian pernicious anemia and that the gastric operation was only incidental. This hypothesis was not tenable in view of the absence of a family history of pernicious anemia and because the histological study of the stomach removed at partial gastrectomy showed normal gastric-body glands and in no way resembled the mucosal atrophy seen in pernicious anemia. The biopsy studies did not allow a detailed comparison between the stomach in this condition and in idiopathic pernicious anemia, but the authors gained the impression that gastritis was present, and they feel that chronic gastritis associated with prolonged dyspepsia, gastric ulceration, and operative intervention may have contributed to the development of gastric atrophy.

Treatment of Lupus Vulgaris with Calciferol Alone: Results After Five Years' Observation. P. V. Marcussen. Danish M. Bull. **2**:129-136 (Sept.) 1955 (In English) [Copenhagen, Denmark].

From 1946 to 1955, 284 patients with lupus vulgaris were treated with calciferol only and regularly controlled. Initial treatment with 4.5 mg. of calciferol daily and individualization of the dose after three weeks resulted in freedom from symptoms in 78.5% of the patients; 16.5% did not become symptom-free, mainly because of intolerance to an effective dose; and 5% lapsed from treatment or died. The late results were disappointing; only 29.2% of the originally treated patients and 37.2% of those who became free from symptoms had not relapsed after an average observation period of five years. There is little advantage in treating patients not cured after the first course of treatment. The treatment of relapsed patients has increasingly less effect, an increasing number of patients becoming intolerant. A total dose of 500-600 mg. of calciferol is generally required, but in some cases 1 gm. or more is needed. The treatment can be carried out without appreciable complications if carefully regulated, especially with regard to blood calcium, blood pressure, and renal function. Pure calciferol treatment with the dosage named is contraindicated in cases of erythema induratum and pulmonary tuberculosis.

Endocrine Organs and Nutrition. H. A. Salvesen. Tidsskr. norske lægefor. **75**:669-672 (Oct. 1) 1955 (In Norwegian) [Oslo, Norway].

The hypophysis occupies the central position among the endocrine organs. A change in its function will affect its target organs: the thyroid, adrenals, gonads, and pancreas. Pituitary insufficiency results readily from undernutrition. The significance of nutrition for the endocrine glands is most evident in the case of the pancreas, and the relation of nutrition to the thyroid is also evident. Excessive administration of calories can cause disturbances of the gonads. The picture of reduced endocrine function must be regarded as a compensation; the organism protects itself against a starvation state by reducing its functions. In over 100 patients with sprue the author found hypotension in all age groups and no case of hypertension. The hypotension is ascribed to an insufficiency of the adrenal cortex that is thought to depend on the nonabsorption of a substance of lipid nature but might be secondary to hypopituitarism. The parathyroid glands suffer from undernutrition in sprue. The direct function of the parathyroids is regulation of the serum calcium; they are stimulated by low serum calcium, and their activity is reduced by a high calcium level. In sprue there is primarily a tendency to hypocalcemia, which explains the tetany that may be the first alarm signal in the disease, but even in the gravest forms of sprue the calcium level may be almost normal. Bone changes in osteomalacia in sprue occur when there is a strong response from the parathyroids. Cases of diabetes may primarily be due to an affection of the pancreas, a pancreatitis, or an atrophy on an arteriosclerotic basis, and in many cases the relation of the liver also plays an important part in the course of the disease, but in the author's opinion diabetes in most cases depends on a hyperactivity of certain functions of the anterior lobe of the hypophysis. The Houssay-Young experiments and the effect of starvation on the diabetic state seem to support the view.

Comparison of the Effect of Four Variables in the Antimicrobial Therapy of Pulmonary Tuberculosis: I. Report of the Cooperative Study of the Veterans Administration, Army, and Navy, April, 1949, to January, 1951. W. B. Tucker. Am. Rev. Tuberc. **72**:718-732 (Dec.) 1955 [New York].

Eight hundred thirteen patients with bacteriologically proved pulmonary tuberculosis, with tubercle bacilli susceptible in vitro to 10γ of streptomycin per cubic centimeter, were admitted in 1949 and 1950 by random allocation to a cooperative investigation of the following comparisons carried out in nearly 50 Army and Navy Veteran Administration hospitals. 1. Daily administration of 1 gm. of streptomycin and 12 gm. of aminosalicylic acid (PAS) for four months was compared with intermittent administration of 1 gm. of streptomycin twice a week and 12 gm. of aminosalicylic acid (PAS) daily for four months. 2. Single-drug therapy with streptomycin or dihydrostreptomycin was compared with "combined therapy" (one or the other of these two antibiotics given daily simultaneously with aminosalicylic acid). 3. Treatment with streptomycin was compared with treatment with dihydrostreptomycin. 4. Combined treatment with streptomycin or dihydrostreptomycin with aminosalicylic acid (PAS) for three months was compared with that for four months. Analysis of defining characteristics showed the comparison groups to be essentially comparable. As judged by roentgenographic improvement, of all degrees or of both moderate and pronounced degree, and by reversal of infectiousness ("conversion" from positive to negative by culture of sputum or gastric aspirates) with follow-up observations up to 12 months after the institution of treatment, the following conclusions may be drawn. 1. Intermittent treatment with streptomycin and aminosalicylic acid (PAS) is as effective as daily treatment with these two drugs. 2. Combined therapy, consisting of administration of either streptomycin or dihydrostreptomycin with aminosalicylic acid (PAS), is slightly superior in its results to treatment with one of the two streptomycin preparations alone, statistically significantly so in some respects. 3. Streptomycin and dihydrostreptomycin are therapeutically equivalent, although they differ in the incidences of their respective toxic reactions for the two branches of the eighth cranial nerve. 4. Antimicrobial therapy with either streptomycin or dihydrostreptomycin and aminosalicylic acid (PAS), both given daily for four months, is superior to such combined therapy given for three months. These results led to the undertaking of a study of prolonged treatment with streptomycin and aminosalicylic acid (PAS) that is reported in the subsequent paper.

Comparative Efficacy of Three Streptomycin and Para-Aminosalicylic Acid Regimens of Prolonged Duration in Patients with Previously Untreated Pulmonary Tuberculosis: II. An Account of the Cooperative Investigation of the Veterans Administration, Army, and Navy, February, 1951, to January, 1952. W. B. Tucker. Am. Rev. Tuberc. **72**:733-755 (Dec.) 1955 [New York].

A controlled investigation was conducted by cooperating hospitals in the Veterans Administration, Army, and Navy, of the relative efficacy of three streptomycin-aminosalicylic acid regimens that were assigned by random allocation to 1,491 patients with bacteriologically proved pulmonary tuberculosis who had not previously received antituberculous chemotherapy. Of the 1,491 patients, 444 were given 1 gm. of streptomycin and 12 gm. of aminosalicylic acid (PAS) daily, 458 received 0.5 gm. of streptomycin and 12 gm. of aminosalicylic acid (PAS) daily, and 589 were given 1 gm. of streptomycin twice weekly and 12 gm. of aminosalicylic acid (PAS) daily. The duration of the therapy varied from 4 to 18 or more months. The three treatment groups were found to be entirely comparable. No significant differences in results of treatment on the three regimens were observed with respect to roentgenographic improvement

of moderate and pronounced degrees, to unfavorable roentgenographic change, to reversal of infectiousness ("conversion" from positive to negative by culture of sputum or gastric aspirates), or to cavity closure rates. This was true not only for the entire group of 1,491 patients but also for all subgroups analyzed according to such characteristics as duration of therapy, extent of disease, and size and number of tuberculous cavities. Combining the results for the three separate streptomycin-aminosalicylic acid (PAS) regimens, in view of the comparability of their results, it was observed that there was a definite relationship between extent of the pulmonary tuberculous disease, as measured either by the National Tuberculosis Association classification or by number and size of tuberculous cavities, and the outcome. As judged by reversal of infectiousness, unfavorable roentgenographic change, and cavity closure rates, the more extensive the disease the less favorable was the outcome. Judged by the criterion of both moderate and pronounced roentgenographic improvement, however, a reverse relationship was noted, with more improvement among those patients with more advanced disease. It has been suggested that this is related to the fact that rapid closing of the larger cavities has an unduly high influence in the interpretation of such "significant" roentgenographic improvement, and, therefore, this criterion is of less prognostic and discriminatory significance. It has proved to be possible by suitable statistical techniques to compare the efficacy of periods of streptomycin-aminosalicylic acid (PAS) therapy of varied durations, even though this variable was not assigned to patients by random allocation. Evidence is presented that streptomycin-aminosalicylic acid (PAS) therapy for a duration of at least 12 months is clearly superior to therapy of 8 or 4 months' duration and that therapy for 18 to 24 months is slightly, if not significantly, superior to that of 12 months' duration.

Isoniazid, Streptomycin, and Para-Aminosalicylic Acid Compared as Two-Drug Regimens in the Treatment of Pulmonary Tuberculosis Among Previously Untreated Patients: III. An Account of the Cooperative Investigation of the Veterans Administration, Army, and Navy, August, 1952, to September, 1954. W. B. Tucker and D. G. Livings. Am. Rev. Tuberc. **72**:756-782 (Dec.) 1955 [New York].

In 2,187 previously untreated patients with bacteriologically proved pulmonary tuberculosis one of the following three regimens was assigned by random allocation: 605 were given 300 mg. of isoniazid daily and 12 gm. of aminosalicylic acid (PAS) daily, 752 received 300 mg. of isoniazid daily and 1 gm. of streptomycin twice weekly, and 830 were given 1 gm. of streptomycin twice weekly and 12 gm. of aminosalicylic acid (PAS) daily. Analysis of factors characterizing the patients and their disease showed the resulting three treatment groups to be highly comparable. The best results, with respect to the criteria reversal of infectiousness ("conversion" from positive to negative by culture of sputum or gastric aspirates), unfavorable roentgenographic change, and cavity closure, were obtained with the isoniazid-aminosalicylic acid (PAS) regimen; the poorest results were obtained with the streptomycin-aminosalicylic acid (PAS) regimen. The results obtained with isoniazid given daily and streptomycin given twice weekly were slightly less good than those obtained with isoniazid and aminosalicylic acid (PAS) administered daily. The more advanced the disease and the greater the cavitary component, the more pronounced was this differentiation. Analysis of the results according to the criterion "significant" roentgenographic improvement (moderate plus pronounced degrees of improvement) showed it to be poorly correlated with the other criteria listed, especially with respect to the stage of the disease and the cavitary component of more advanced disease. It is concluded, therefore, that the criterion "significant" roentgenographic improvement is of restricted value in such studies and that greater reliance should be placed on other more objective measures. Regarding the influence of variables other than those of the antimicrobial drugs employed, evidence has been presented that indicates that race and age per se do not appear to be clearly associated with outcome, that results are less satisfactory the more advanced the disease and the larger its cavitary component at the institution of therapy, and that patients with bilateral involvement respond less well than those with unilateral. It has not been possible to analyze the relative influence of differing durations of therapy. Most of the patients were treated for more than 12 months, but the evidence continues to suggest that 12 months of therapy is the minimum advisable and that more may be advisable in most patients. Data have been presented that indicate that, when either isoniazid or aminosalicylic acid (PAS) is administered daily in combination with streptomycin twice weekly, rates for the emergence of streptomycin-resistant strains of tubercle bacilli are comparable. When aminosalicylic acid (PAS) given daily is compared with streptomycin given twice weekly in combination with isoniazid given daily, however, the rates for the emergence of drug-resistant organisms (resistant in vitro to isoniazid concentrations of 5 mcg. per cubic centimeter) are significantly higher for the daily isoniazid and twice-weekly streptomycin regimen. Reference has been made to the fact that the clinical significance of this finding is not clearly established. Comparison of the results of the cooperative investigations of the Veterans Administration, Army, and Navy, with those of the British Medical Research Council and the second isoniazid study of the United States Public Health Service showed good agreement in that regimens that employ isoniazid in combination with either streptomycin or aminosalicylic acid (PAS) are about equally effective but that streptomycin given twice weekly in combination with isoniazid is slightly less effective than the combination of isoniazid and aminosalicylic acid (PAS). The British Medical Research Council trials have indicated that the combination of isoniazid given daily and streptomycin administered daily consistently gives the best results. There is increasing evidence that the final decision as to what antimicrobial therapy will be prescribed in practical clinical application will depend on variations of the disease and on other factors not included in the large-scale British and United States cooperative studies.

SURGERY

Total Excision of the Aortic Arch for Aneurysm. D. A. Cooley, D. E. Mahaffey and M. E. De Bakey. Surg. Gynec. & Obst. **101**:667-672 (Dec.) 1955 [Chicago].

Excisional therapy for aneurysms of the aorta is now established as the method of choice. For fusiform aneurysms this procedure involves cross clamping the aorta above and below the diseased segment following which the lesion is excised and circulatory continuity is restored by means of an aortic homograft or prosthesis. Temporary arrest of aortic circulation thus becomes the major hazard. This is particularly true for lesions lying in the aortic arch and requiring temporary occlusion of the ascending aorta. The two major obstacles under these circumstances are ischemic damage to the brain and spinal cord and cardiac failure from left ventricular strain. To overcome these problems two measures may be employed, namely, hypothermia and bypass shunts. A case is reported in which total excision of the aortic arch was performed followed by replacement with a prosthesis made of compressed polyvinyl sponge (Ivalon). The patient survived six days, during which period the prosthesis functioned well. The combined use of hypothermia and bypass shunts in this particular case is considered to have contributed materially to the feasibility of the procedure. Death of the patient six days after operation was due to cerebral damage from temporary ischemia resulting from thrombosis of the right carotid shunt that occurred during the insertion of the Ivalon prosthesis. Approximately eight minutes elapsed from the time the thrombosis in the shunt was recognized until the clamp on the ascending aorta was released and carotid flow was reestablished. Perhaps such technical complications of the procedure could be avoided by use of heparin either locally or systemically or preferably by siliconizing the inside of the tubes. Except for the accident that subsequently led to death of the patient, the operation was performed without great difficulty. The fact that the patient survived the operation and lived for six days, during which time all peripheral pulses were readily palpable, testifies to the feasibility of total arch resection from a technical standpoint and justifies further attempts of this kind.

Indications for Operation in Chronic Constrictive Pericarditis. C. Dubost and C. d'Allaines. J. chir. **71**:852-869 (Nov.) 1955 (In French) [Paris, France].

Sixty-two cardiac decortications were performed for chronic constrictive pericarditis in 53 patients. The patients were followed up for at least six months after operation. Thirteen died during or immediately after operation, a rate of 20.9%. Four could not be traced, and of the remaining 36, 29 (54.7%) had good or excellent results. All of these returned to normal activities. Six patients obtained partial improvement and one no improvement. Those who were operated on more than once needed reintervention because of insufficient resection and not because constriction reappeared in the parts formerly freed. The only definitive treatment for constrictive pericarditis is pericardectomy, but there are certain limitations to the indications for this operation. It cannot be proposed for patients whose general condition is very poor. In some instances it can be deferred until the condition has been improved. There is no point in using the operation in patients, especially those over 40, who tolerate their disease well after it has become calcified and stabilized and is no longer active. The optimal time to operate is when inflammatory activity has ceased and constriction has set in, but not myocardial failure; this is normally the situation at between 10 and 18 months after the apparent onset of the illness. The mechanical reason the pericardium must be removed is because it causes ventricular adiastole; thus it would seem that only the ventricles need be liberated, but this is actually not the case. The sac also presses on the atria, especially on the terminations of the venae cavae. However, liberation of all parts of the heart except the right atrium is as effective as total pericardectomy. Besides the ventricles, it is also indispensable to free the interventricular and right atrioventricular sulci, as well as the origin of the basal arterial vessels. The best route to use in this operation is the left transpleural with horizontal sternotomy. The thoracotomy is made in the fourth intercostal space or over the fourth rib.

Spontaneous Rupture of the Esophagus: A Not Uncommon Medical Emergency. W. K. Swann, J. T. Bradsher, T. L. Lomasney and W. C. Retterbush. J. Tennessee M. A. **48**:407-410 (Nov.) 1955 [Nashville, Tennessee].

Four cases of spontaneous rupture of the esophagus are described in three men aged 45, 66, and 62 years, respectively, and in a 79-year-old woman. Their occurring in one medical community within the brief period of two years suggests that spontaneous rupture of the esophagus is a not uncommon medical emergency. All patients had agonizing chest pain after spontaneous or self-induced vomiting. Three of the patients died with a diagnosis of myocardial infarction; surgical consultation was not sought, and the correct diagnosis was not established until autopsy was done. A preoperative diagnosis of spontaneous rupture of the esophagus was made in one patient in whom auscultation of the thorax revealed crepitant rales over the left lower chest and subcutaneous emphysema was palpable in the left side of the neck. A posteroanterior roentgenogram of the chest in the erect position revealed a minimal pleural effusion at the left base and mediastinal emphysema. Thoracotomy was performed, a gastric tube was passed into the stomach, and a 3 cm. longitudinal rent in the esophagus in the left posterolateral wall just above the gastric cardia was closed over the tube in two layers by interrupted silk sutures. On the sixth postoperative day delirium tremens developed from which the patient, a periodic alcoholic, recovered after three days of treatment with corticotropin (ACTH) and sedatives. He was discharged on the 10th postoperative day. Failure to make a correct diagnosis in a case of spontaneous esophageal rupture is usually not attributable to a paucity of characteristic findings but can most often be ascribed to a lack of familiarity with the syndrome or a failure to keep it in mind in the differential diagnosis of severe chest pain. A patient presenting prostrating chest pain, subcutaneous emphysema, and hydropneumothorax has almost certainly suffered rupture of the esophagus. The diagnosis should be suspected before appearance of emphysema and hydrothorax in a patient who has agonizing chest pain after the act of vomiting, which may or may not have followed overindulgence in food or alcohol. The correct diagnosis is usually arrived at with the aid of the history, physical examination, and chest roentgenograms made in the erect position. Confirmation may be obtained by aspirating liquid or solid food material from the pleural space, aspirating methylene blue previously given by mouth, or giving a swallow of iodized oil whose escape into the mediastinum or pleural space may be shown by roentgenograms. Recognized early and treated promptly by surgical closure, spontaneous rupture of the esophagus is curable. Untreated it is almost always fatal.

Endocrine Treatment of Metastatic Breast Cancer. O. H. Pearson, C. D. West, J. P. McLean and M. B. Lipsett. Am. Surgeon **21**:1075-1083 (Nov.) 1955 [Baltimore].

A review of the literature showed that of 75 premenopausal women with metastatic breast cancer who underwent oophorectomy, 33 (44%) obtained objective remissions of their disease. The average duration of the remissions was nine months. Metastases to nearly every organ were observed to regress after oophorectomy. Of 21 postmenopausal women with metastatic cancer of the breast, only 2 (10%) obtained objective remissions after oophorectomy. Among 38 women with metastatic cancer of the breast all of whom had previously undergone oophorectomy, bilateral adrenalectomy produced objective remissions in 17 (45%); the average duration of the remission was 8.5 months. Combined oophorectomy and bilateral adrenalectomy was performed in 25 postmenopausal women with metastatic breast cancer, and 16 of these patients obtained objective remissions with an average duration of more than seven months. Oophorectomy is the initial treatment of choice in premenopausal women with metastatic breast cancer; in premenopausal patients who have responded to oophorectomy and then relapsed, adrenalectomy is the treatment of choice. In postmenopausal women, combined oophorectomy and adrenalectomy is the recommended initial therapy. Of 30 patients with metastatic breast cancer who underwent hypophysectomy after previous endocrine therapy consisting of oophorectomy and adrenalectomy, 16 (53%) obtained objective remissions after hypophysectomy. Further experience with hypophysectomy in the treatment of advanced cancer of the breast is required before a final appraisal can be made, but preliminary observations suggest that hypophysectomy may offer the optimum endocrine therapy for these patients. Results of androgen therapy with testosterone propionate in doses of 100 mg. three times per week in 54 premenopausal and in 113 postmenopausal women showed that the percentage of remissions obtained with androgen therapy was less than that obtained with oophorectomy and adrenalectomy. Since androgen therapy also carries the potential of exacerbating the growth of breast cancer, it would seem logical to reserve androgen therapy until the disease has relapsed after oophorectomy and adrenalectomy. The administration of estrogens to 76 postmenopausal patients with metastatic breast cancer produced objective remissions in 24 (32%). Estrogen administration, however, appeared to accelerate the course of the disease in 50% of women of all age groups. Because of this potential harmful effect of estrogen, it would seem wise to restrict its therapeutic use to those patients who fail to respond to oophorectomy or to oophorectomy combined with adrenalectomy. Estrogen therapy should be tried cautiously in patients in whom ablative procedures cannot be done. Since remissions induced by cortisone were of short duration, it seems best to reserve this therapy for patients who fail to respond to the other methods of endocrine therapy or who relapse after such therapy. The mechanisms by which alterations in the hormonal environment affect the growth of mammary cancer are discussed and a physiological concept for treatment is presented.

Prescalene and Deep Cervical Lymph Node Biopsy. R. G. Connar. Surg. Gynec. & Obst. **101**:733-743 (Dec.) 1955 [Chicago].

A study was undertaken to estimate (1) the practical value of a prescalene biopsy in establishing the diagnosis in patients with previously undiagnosed intrathoracic lesions and (2) the value of the procedure in preventing unnecessary thoracotomies in patients with carcinoma of the lung, i. e., when the malignancy has already spread beyond the limits of surgical excision. The author describes the technique of the biopsy. He performed prescalene and deep cervical lymph node biopsies in 50 consecu-

tive patients with previously undiagnosed intrathoracic lesions. Positive tissue diagnosis was established by prescalene and deep cervical lymph node biopsy in nine cases of carcinoma of the lung, four cases of Boeck's sarcoid, and one case of Hodgkin's disease. The incidence of a positive tissue diagnosis was the same (31%) as by bronchoscopic biopsy. Undifferentiated carcinoma was the most commonly encountered malignant disease in the prescalene and deep cervical lymph node biopsies. There was a high incidence of positive biopsy findings in cases of Boeck's sarcoid. If the prescalene and deep cervical lymph node biopsy is positive in the case of carcinoma of the lung, exploration should be reserved as palliation for major hemorrhage or infection.

The Clinical Value of Colonic Exfoliative Cytology in the Diagnosis of Cancer Beyond the Reach of the Proctoscope. J. T. Galambos and M. I. Klayman. Surg. Gynec. & Obst. **101**:673-679 (Dec.) 1955 [Chicago].

The authors describe their experience with colonic exfoliative cytological studies on 68 patients in whom a colonic lesion beyond the reach of the proctoscope was suspected clinically. Two different techniques were used. In 20 patients who were examined during the first nine months of this study only Ringer's solution was used as an irrigating fluid; the return was immediately searched for blood-tinged mucus and mucous shreds, which were smeared on slides thinly coated with Mayer's albumin, fixed in ether-alcohol and stained. In the 48 patients examined during the last nine months of this study the initial rapid washing with Ringer's solution was followed by 500 to 1,000 cc. of acetate buffer with 14 to 21 mg. of salt-free chymotrypsin enema that was retained for 5 to 10 minutes. The return was collected in iced containers and then was centrifuged at 5,000 revolutions per minute for three minutes. The sediment was smeared on slides thinly coated with Mayer's albumin. These were then fixed and stained. Follow-up information was available in 59 of the 68 patients. In 26 patients malignant lesions were found at operation. The correct diagnosis was established by colonic exfoliative cytological studies in 16 patients. There was a marked increase in the diagnostic accuracy during the last nine months of the study following changes in technique. One case of metastatic ovarian carcinoma was correctly diagnosed by cytology. One patient in whom malignant cells were found and in whom carcinoma of the sigmoid was diagnosed by x-ray study refused surgery. There were no false-positive reports in 32 cases in which malignancy was excluded (by surgery in 14 and by clinical observation in 18 cases). Nine patients in whom no malignant cells were found could not be reached for follow-up. The authors conclude that in experienced hands colonic exfoliative cytology is a valuable adjunct in the diagnosis of colonic lesions. The demonstration of malignant cells is conclusive evidence for carcinoma, although their absence does not exclude its presence.

Surgical Elimination of Foci in Chronic Carriers of Eberthella Typhosa: Report on 102 Patients Operated On. W. Anders, F. Linder and W. Stephan. Deutsche med. Wchnschr. **80**:1637-1640 (Nov. 11) 1955 (In German) [Stuttgart, Germany].

Of 102 chronic carriers of Eberthella typhosa on whom cholecystectomy was performed at the surgical clinic of the Free University of West Berlin between 1946 and 1954, only one patient died. The operation was successful in 91 patients who either could be definitively dropped from the list of chronic carriers or from whose feces the causative agent could not be cultured postoperatively for one year during which bacteriological examinations were made at regular intervals. This favorable result was obtained by the proper selection of chronic carriers for surgical intervention. The following rules were observed. 1. Symptoms that may suggest a disease of the gallbladder, such as intolerance of certain foods, abdominal pains, or attacks of jaundice, must be searched for. 2. Surgical intervention must be preceded by the following examinations: examination of feces, which shows that the causative agent is excreted exclusively in the feces; bacteriological control of catheter-urine, required to exclude patients who excrete the causative agent in the urine; clinical and bacteriological examination of the duodenal juice with the aid of the duodenal tube; and roentgenologic examination of the gallbladder (surgical intervention is indicated when a negative cholecystogram is obtained, when calculi are visualized, or when considerable functional disturbances of the gallbladder are shown). 3. The time of choice for the operation is one of absence of an acute disease of the gallbladder. Removal of the gallbladder in the presence of acute disease makes the prospect of elimination of carrier foci less favorable. 4. Advanced age or associated diseases may present contraindications; patients over 60 years of age and patients with cardiac decompensation or valvular defects may be operated on only in exceptional cases. Cholecystectomy should be recommended to the chronic carrier only when all these rules have been fulfilled. Conservative treatment should be practiced during an acute exacerbation of gallbladder disease, and surgical intervention should be postponed. Prolonged observation of the patient must precede surgical intervention in every instance. The authors disapprove of routine postoperative treatment with chloramphenicol or other antibiotics; in exceptional cases antibiotic treatment may be required but then recolonization of the intestine should be carried out with coli bacilli that are antagonistic to Eberthella typhosa.

Clinical Experiences with Combined Therapy with Antibiotics and Omnadin (Omnamycin) in Surgery. H.-G. Timmer. München. med. Wchnschr. **97**:1537-1539 (Nov. 18) 1955 (In German) [Munich, Germany].

Sixty-five surgical patients were treated with Omnamycin, a proprietary preparation containing penicillin, dihydrostreptomycin, and Omnadin, a mixture of reactive protein bodies from various nonpathogenic fungi with lipoids from bile and from other animal fats. Thirty-four surgical patients who were given combined treatment with penicillin and streptomycin served as controls. Omnamycin was given to combat suppurative inflammation, as a prophylactic in patients subjected to laparotomy or in those with complicated fractures, in surgical treatment of fractures and other serious conditions, and for the treatment of wounds. In general one ampul of the drug was given every 24 hours; patients running a high temperature were given one ampul every 12 hours. As a rule treatment was continued for six days, and occasionally for longer periods, but always for two more days after the temperature had been restored to normal. Of the 65 patients, 13 had no fever when treatment was instituted. The remaining 52 patients had fever and in all of them temperature was restored to normal within an average period of four days. Among the 52 patients there were 12 with fever of 38 C (100.4 F) to 38.5 C (101.2 F). Restoration of temperature to normal on the third to the fifth day after the institution of the treatment with Omnamycin is characteristic and occurred in all but three patients; two of these, one with cystitis resulting from hypertrophy of the prostate and the other with peritonitis following total gastric resection, cannot be considered therapeutic failures, because of the peculiarities of their cases. In the third patient, who had traumatic empyema of the knee joint, temperature was restored to normal on the 10th day. Of the 34 control patients, 6 did not have fever when treatment with penicillin and streptomycin was instituted; in the remaining 28 patients with fever, temperature was restored to normal on the seventh or eighth day only. This "critical" defervescence after the administration of Omnamycin appears to depend on the Omnadin, which does not cause a rise of temperature. Besides its prompt influence on fever and on the general condition, Omnamycin also shortens the course of the disease. The advantages of Omnamycin therapy compared with the results of penicillin-streptomycin therapy are emphasized.

The Uptake of Labelled Sulphate Injected into the Host Animal by Cartilage Homografts. G. M. Wyburn and P. Bacsich. Brit. J. Plast. Surg. **8**:177-185 (Oct.) 1955 [Edinburgh, Scotland].

There is ample experimental and clinical evidence that fresh cartilage homografts survive for long periods, e. g., man, three years; rabbit, 18 months; and dog, 18 months. Histologically the chondrocytes remain alive in cartilage homografts, although there is a temporary change in their metabolism indicated by a decrease in lipid and glycogen content of the cells within 14 days. The ground substance retains its metachromasia, which is regarded as a reliable quantitative test for the presence of ester

sulfate of high molecular weight such as chondroitin sulfate, a characteristic constituent of healthy viable cartilage matrix. The metabolism of cartilage, which means the activity of the chondrocytes, is concerned with the "turnover" of ground substance including chondroitin sulfate. Direct evidence of this metabolic activity can be obtained by the uptake of labeled sulfate ($^{35}SO_4$) by living cartilage, which is organically bound in its chondroitin sulfate. The studies described in this paper concerned the assimilation by cartilaginous homografts of the radioactive sulfate, $^{35}SO_4$, injected into the host animal. A graft of xiphoid cartilage was inserted subcutaneously into each of four adult guinea pigs and similarly a graft of costal cartilage into each of four additional animals. Three weeks after the insertion of the graft the host animal was given a subcutaneous injection of 5 mc. of $^{35}SO_4$ at pH 5. The animals were killed and the grafts recovered 24 hours after this injection. The grafts, together with control specimens of the xiphoid and costal cartilage of the host animal, were fixed for one hour in a mixture (3 to 1) of absolute alcohol and acetic acid and subsequently for 24 hours in formol saline. After paraffin embedding, 5μ sections of controls and cartilage were cut. A number of sections from each block were prepared for autoradiography by the stripping film technique, with an exposure of about 42 days. After development, fixation, and drying, the autoradiographs were photographed. Other sections were stained with hemalum and eosin or with a 0.5% aqueous solution of toluidine blue. The results of these studies provide direct evidence that cartilage can survive as a homograft and prove that the histological criteria of viability denote an actively metabolizing tissue. The similarity in the appearance of the control and graft autoradiographs justifies the conclusion that the graft has established normal nutritional relations with the host tissue and a "turnover" of ground substance parallel to that of the host cartilage. The uptake of labeled sulfate is suppressed by cyanide poisoning or by heat. It is therefore an active cellular process and so, despite its avascularity, the relative intensity of cartilage autoradiographs indicates an active metabolism concerned with the breakdown and continuous new formation of chondroitin sulfate.

Acute Cardiac Tamponade, a Complication of Sternal Marrow Aspiration: Report of a Case. L. B. Jenkins, B. E. Ferrara and H. P. Snead. A. M. A. Arch. Surg. 71:892-895 (Dec.) 1955 [Chicago].

The first reported case of cardiac tamponade after sternal marrow aspiration successfully treated is described in a 24-year-old Negro man with chronic glomerulonephritis, secondary hypertension, and pronounced anemia. Because of the anemia a sternal bone-marrow aspiration was done. No difficulty was observed. The specimen obtained was reported as peripheral blood. Four days later the sternal marrow aspiration was repeated with a 16-gauge, short-beveled, 1.25 in. marrow needle. The procedure was done in the midsternal line 1 cm. below the site of the previous aspiration. No difficulty was noted, but the surgeon had directed the needle "more deeply in order to avoid obtaining another sample of peripheral blood." One hour after the sternal puncture, the patient vomited and complained of pain in the sternal area, made worse by breathing. Six hours passed before the classical syndrome of quiet-heart, venous distention, and hypotension developed. In 13 patients collected from the literature who died after sternal marrow aspiration, the same syndrome developed and death resulted within 10 to 30 minutes. Removal of 215 cc. of blood from the pericardium by two pericardiocenteses, with an interval of eight hours between the two, relieved the cardiac tamponade in the authors' patient but the patient died 23 days later of progression of his chronic glomerulonephritis with hypertension and renal failure. Permission for autopsy was not obtained, but the delay in the appearance of the typical signs and symptoms of cardiac tamponade suggests that the source of the intrapericardial blood was a site of low pressure oozing. Such a site could have been injury to the auricles, intrapericardial veins, retrosternal veins, or the sternum itself, with a laceration of the pericardium only. The prevention of such a complication as cardiac tamponade after sternal puncture requires strict avoidance of the exertion of force. The impulse to penetrate deeper if difficulty is experienced in obtaining marrow blood must be repressed. Performing sternal puncture as high on the sternum as possible, angulation of the needle into the manubrium, or extreme care at a site softened by disease may be safety factors of importance if a needle is used. The safety of the routine use of the trephine-type instrument for sternal puncture, and particularly for multiple aspirations, has been emphasized. Any patient exhibiting signs and symptoms of a failing circulation after sternal puncture should have immediate pericardiocentesis to exclude the possibility of cardiac tamponade and to treat it if present.

Spontaneous Pneumothorax, a Review with the Results of Pulmonary Resection in Nineteen Patients. J. L. Ehrenhaft, R. E. Taber and M. S. Lawrence. Am. Rev. Tuberc. 72:801-809 (Dec.) 1955 [New York].

Fifty-two patients with spontaneous pneumothorax were admitted to the State University of Iowa Hospitals between 1938 and 1955. Nineteen of these were subjected to thoracotomy and resection of ruptured subpleural blebs. Wedge excision was performed in 16 of these patients, segmental excision in 2, and lobectomy in one. Of the remaining 33 patients, 12 were treated with intercostal underwater seal drainage, 7 with needle aspiration of air, and 14 were observed for an average of 21 days in the hospital but did not receive any specific treatment. Thoracotomy and excision of the ruptured subpleural blebs resulted in a short hospital stay of 12 days on the average, with no morbidity or mortality. All 19 patients were discharged with completely expanded lungs. Recurrences of pneumothorax were not observed in the patients treated in this manner. In contrast, the patients treated with intercostal underwater seal drainage, needle aspiration, or those only observed in the hospital were hospitalized for a longer period and had a high recurrence rate. Three patients in the nonresected group died; death resulted from untreated tension pneumothorax in two and from inadequate intercostal drainage in one patient with bilateral pneumothorax. Repetitive and severe tension pneumothorax, as well as hemopneumothorax, should be treated by immediate exploratory thoracotomy. Visualization of subpleural blebs in a spontaneous pneumothorax in chest roentgenograms also constitutes an indication for their excision. Underwater seal drainage may be employed in initial and minimal degrees of pneumothorax. It must also be used as an emergency measure in patients with tension or bilateral pneumothorax. Needle aspiration and expectant management seldom result in prompt and complete reexpansion of the lung. The recurrence rate is high with this type of treatment. Thoracotomy and excision of ruptured subpleural blebs provide for eradication of the lesion and result in prompt and complete expansion of the lungs. This form of treatment prevented further recurrences of pneumothorax in the authors' patients.

Suture Control of Bleeding Duodenal Ulcer: A Safer Approach in the Treatment of the Critically Ill Patient. H. L. Albright and R. C. Kerr. A. M. A. Arch. Surg. 71:803-808 (Dec.) 1955 [Chicago].

Seven patients between the ages of 46 and 68 years with bleeding duodenal ulcer were treated by adequate direct suture of the bleeding ulcer. The procedure consisted of a generous incision vertically through the midline or the left rectus in the upper abdomen, then extending across and down to the right of the umbilicus. After palpation of the ulcer a longitudinal incision opening the antrum, pylorus, and duodenum was made. The authors do not hesitate to divide the pylorus and feel that wide exposure is one of the key factors in the success of this procedure. Hemostatic sutures were placed on each side of the incision, and the wall of the intestine was incised to expose the ulcer. Multiple figure-of-eight sutures of cotton were placed in the ulcer bed to control bleeding adequately. If the patient's blood pressure is depressed at this point, pressure should be restored before the intestine is closed, to be sure that the bleeding is completely controlled when pressure is normal. Closure was made in the Heineke-Mikulicz manner at the duodenal end of the incision, with simple reapproximation of layers of the gastric portion. In six of the seven patients the blood pressure immediately returned to and stayed normal, and no

further bleeding occurred. One patient, who showed evidence of further bleeding after the surgical intervention, died on the sixth postoperative day; permission for autopsy was not obtained. The six surviving patients resumed normal activities, four having had definitive surgical intervention at a later date. The remaining two have gone 9 months and 14 months, respectively, without further bleeding. These results indicate that adequate direct suture of the bleeding ulcer is a satisfactory method of stopping blood loss, which is the sole requirement of emergency surgery in these poorest-risk patients. Gastrojejunostomy is not needed, for pyloric obstruction is avoided by transverse closure of the pyloric portion of the longitudinal visceral incision. The simplicity of this method renders it much safer than subtotal gastrectomy with or without excision of the ulcer.

Adrenalectomy in Metastatic Breast Cancer: A Report of Six Cases. W. E. A. Hughes-Jones. M. J. Australia 2:762-764 (Nov. 5) 1955 [Sydney, Australia].

The first two of the six patients presented are examples of infiltration and metastases in the soft tissues. In the first patient, a woman, aged 28, adrenalectomy and oophorectomy made not the least alteration in the course of the cancer, nor in the soft-tissue lesions. In the second patient, a 51-year-old woman, the first opinion of the radiologist that there was carcinomatous infiltration of the lungs was correct, and there were pleural metastases in addition. The oophorectomy and adrenalectomy were performed at an early stage of this dissemination, and yet the course of the disease was not altered. The remaining four patients had metastatic infiltration of the skeleton. Their ages ranged from 35 to 56 years. One of these died 48 hours after adrenalectomy. In another there was not the slightest response to adrenalectomy. In still another removal of the ovaries and adrenals performed just over a year prior to death did not seem to have made any appreciable difference in the course of the disease, apart from the fact that the patient had no pain. This case was an example of slowly progressing skeletal involvement in metastases. In the fourth patient with skeletal metastases (the last of the group of six), the progress was extremely slow, the course of the carcinoma and metastases being at least nine years. In this patient sclerotic lesions were widespread in the skeletal system after bilateral oophorectomy and adrenalectomy. Sclerosis does not imply healing. It is a characteristic of the life history of the skeletal metastases in some patients, the bones becoming heavier and denser, just as rarefaction is a characteristic in other patients. The author concludes that, in these six patients with metastases from breast cancers, removal of the adrenals and ovaries had no apparent effect on the course of the life history of the disease.

Polyps and Pigment in the Peutz-Jeghers Syndrome. J. T. Freeman and I. S. Ravdin. New England J. Med. 253:958-961 (Dec. 1) 1955 [Boston].

The clinical condition described by Peutz of Holland in 1921 was characterized by him as a familial polyposis of the mucosa of the small intestine with unusual skin and mucosal pigmentations. Jeghers reported the history of a patient with this syndrome in 1944 and reviewed the world literature. Since Jegher's interest is primarily responsible for calling attention to this syndrome, the authors of this paper agree with Bruwer and others of the Mayo Clinic that "if an eponymous title is to be attached to this syndrome, it would seem fair to call it the Peutz-Jeghers syndrome." They present the history of another patient, in whom melanin deposits in the skin and buccal mucosa were associated with polyposis of the small intestine. His father died at the age of 28, having had similar spots on his lips, and the widow said that it was her understanding that her husband had died of an obstruction of the intestines, on the basis of cancer. In 1942, when the patient was 23 years of age he was operated on for bilateral inguinal hernia. Clinical study in 1952 suggested that the patient was anemic. An episode of nausea, vomiting, and diarrhea at about this time responded to the usual measures. He was not seen again until two years later, when he had a similar bout and when there was tenderness and a suggestion of a mass in the right lower abdominal quadrant. X-ray study of the digestive tract was interpreted as showing the scar of duodenal ulceration, some irritation of the mucosa of the descending colon, and the possibility of adhesions in the region of the ileum. Owing to a bizarre sensation over the cecum, the intention of exploring this area was stated before the operation. The history revealed repeated attacks of abdominal cramps lasting for several hours, always subsiding without residual effects, for the last three years. Operation revealed a large pedunculated polyp about 15 cm. from the ileocecal valve. About 35 cm. proximal to this lesion there was a segment of intestine, approximately 30 cm. in length and containing two large polyps, about which the small intestine had become intussuscepted. Between these two locations there were several small polyps. The area of the larger polyps seemed suspicious because of involvement of the serosa of the intestine. The entire segment of the intestine, including the polyps and a generous wedge of mesentery down to its root, was resected. An end-to-end anastomosis was performed. A single polyp located more distally near the ileocecal valve was removed and the intestine closed. The postoperative course was uneventful. Two of the polyps had undergone malignant change. Convalescence was slow. The patient began to take a preparation of iron by mouth; he reported improvement in his strength and well-being. A year later he was still well and had gained weight. Anemia was detected in 11 of the 16 patients with the Peutz-Jeghers syndrome whose histories mention blood studies.

GYNECOLOGY & OBSTETRICS

Diverticulum of the Female Urethra. J. R. Kight and N. N Hill Jr. Am. J. Obst. & Gynec. 70:1214-1217 (Dec.) 1955 [St. Louis].

The authors observed 15 patients with urethral diverticula. Their report is based on 10 of these cases. The symptoms of this condition may be severe and intermittently incapacitating. The patients had received many kinds of treatment prior to establishment of the correct diagnosis. The interval between onset of symptoms and correct diagnosis ranged from months to many years, and the therapy had consisted of medical and surgical measures. It is now generally believed that true or congenital diverticula do occur, but the acquired type is much more common. It arises in the periurethral ducts and glands present throughout the length of the urethra. The authors believe the acquired type may develop as a result of intraurethral pressure in association with one of the following processes: (1) infection of a periurethral duct or gland, (2) injury to the urethral mucosa and abscess formation such as may occur from instrumentation, electrocoagulation, or passage of a calculus, and (3) rupture of a periurethral cyst or abscess, which may or may not have had its origin in a periurethral gland, due to a force arising in the vagina. Pressure associated with childbearing has long been considered causative. The size of a diverticulum of the urethra may vary from a minute structure to a mass filling the anterior portion of the vagina. It may be situated just beneath or lateral to the urethra. Occasionally it is elongated and extends upward beneath the bladder. Most diverticula open into the middle or posterior third of the urethra, usually into the vaginal half of the circumference, rarely into the subpubic half. Calculi are frequently found in diverticula and were present in 2 of the 10 patients reviewed. Pain in the region of the urethra, more marked at the time of or immediately after voiding, was the chief complaint in the majority of cases. Leakage of urine or purulent material after voiding was frequently an associated complaint. A definite diagnosis of a diverticulum may be established by one of three methods. First, the opening may be visualized through the cystoscope or panendoscope. Digital pressure on the vaginal wall at the time of cystoscopy may aid in locating the entrance of the sac. A second method consists of performing a urethrogram. The third method, diagnosis by exploration alone, is not recommended, because of the possibility of the existence of an ectopic ureter. Since a urethral diverticulum is a collapsible sac, which may at times be temporarily occluded, the diagnosis may be difficult even when the condition is suspected. The authors found the urethrographic method the most satisfactory one, and they recommend that x-ray studies of the

urethra be done in all cases prior to surgical treatment. Excision of the sac and closure of the urethral opening constitute the procedure of choice.

Hydrotubation: Separate Examination of the Patency of Each Tube with Isotonic Saline Solution. H. Yagi. Fertil. and Steril. 6:550-556 (Nov.-Dec.) 1955 [New York].

The term hydrotubation was introduced by Yagi in 1929 to describe a new technique for diagnosing patency of the fallopian tubes by means of sodium chloride solution instead of air or carbon dioxide. The idea came to him in performing hysterosalpingographies. He noticed that, when more than 10 cc. of iodized oil can be injected easily under low manometric pressure, it is almost a positive indication that one or both of the tubes are patent. If there is a tubal closure or stenosis, resistance is encountered, and, when added pressure is applied, oil will leak from the uterus into the vagina. This led the author to conclude that tubal patency could be tested with the use of a nonradiopaque medium such as sodium chloride solution, without the aid of x-ray pictures. Sodium chloride solution, at body temperature, is an ideal nonirritating medium. Its use is free from the potentially dangerous after-effects, notably embolism, that are sometimes associated with the use of radiopaque oils. The solution is introduced from a cylinder in such a way that its upper level is 2 m. above the uterus. By noting the quantity and speed of flow, the degree of tubal patency can be estimated. In 1944 the author worked out a new technique for the separate hydrotubation of the individual tubes. The principle of the new method lies in blocking one of the fallopian tubes at its uterine cornu with the tip of a special cannula, which resembles the end of a uterine sound, and then injecting the sodium chloride solution into the other tube through openings below the tip of the cannula. During the past 20 years the author performed 3,000 hydrotubations with accurate diagnoses in 95% of the cases, as determined by follow-up with laparotomy or by hysterosalpingograms.

Complete Perineotomy. C. B. Cunningham and J. W. Pilkington. Am. J. Obst. & Gynec. 70:1225-1231 (Dec.) 1955 [St. Louis].

The authors define complete perineotomy as the deliberate extension through the sphincter ani or into the rectum of a median episiotomy (perineotomy). Years ago an extension of a perineal laceration into the rectum was considered to be a catastrophy. Therefore lateral and mediolateral episiotomies were done in spite of the fact that nature always placed her episiotomy in the midline. The routine median episiotomy leads to extensions and lacerations of the rectum more frequently than the mediolateral episiotomy, but these lacerations when properly repaired heal well and appear better post partum than perineotomies of lesser degree. This the authors attribute to the fact that the tissues break before they are overstretched. They practiced deliberate incision of the sphincter ani and rectal wall when rupture seemed imminent. They performed this complete perineotomy in 31 of 290 primiparas. They make multiple midperineal snips. These incisions are carried to the sphincter ani externus fascia and well up the vaginal wall. As the head is brought toward the perineum, the sphincter ani externus and the rectal wall are watched for stress. For example, when the rectum is dilated 3 to 4 cm. the head is then allowed to recede, the sphincter ani externus and the rectal wall are incised, and delivery is carried out. Age was not a contributing factor in necessitating complete perineotomy. However, the average birth weight was larger in cases in which complete perineotomy was required. The authors believe that large babies, short perineums, and narrow forepelves are indications for complete perineotomy; any one or all of these factors may be operative in any given case. The patients undergoing median episiotomies had far less perineal discomfort than other primiparas who had been subjected to mediolateral episiotomies; none had wound sepsis, sphincter paralysis, rectovaginal abscess or fistula, or rectal incontinence. Furthermore, there is more sensitivity and subsequent dyspareunia in the mediolateral scar, as multiparas who have experienced both types can testify.

PEDIATRICS

Staphylococcal Empyema. G. M. Brownrigg. Canad. M. A. J. 73:787-789 (Nov. 15) 1955 [Toronto, Canada].

Seventeen cases of pneumonia in infants and children, all caused by a penicillin-resistant Micrococcus (Staphylococcus) were observed on the pediatric and surgical services of the St. John's General and St. Clare's Mercy Hospitals in Newfoundland, Canada. In 13 of the 17 patients the diagnosis was established clinically and adequate treatment was employed with properly selected antibiotics and drainage of empyema. Only one of these 13 patients, a 4½-month-old infant, died; autopsy confirmed the presence of empyema and bronchopleural fistula communicating with a lung abscess. In four additional infants, the presence of abscess, bronchopleural fistula, and empyema was not established clinically but was revealed by autopsy. The development of this complication was rapid but nonetheless insidious and difficult to recognize. All the patients were critically ill with respiratory distress and cyanosis; the development of fistula, pneumothorax, and empyema frequently caused little obvious change in the patient's condition. Early diagnosis and adequate treatment by a properly selected antibiotic and the prompt surgical treatment of complicating empyema with tube drainage with a closed underwater system to which suction may be added, intercostal drainage, or rib resection can bring about a dramatic reduction in mortality rate. There is no place for the employment of repeated aspiration as a method of treatment. In the author's patients, chloramphenicol was the most effective drug; in vitro sensitivity tests are essential to determine the drug of choice in the individual patient. Rapid change in drug sensitivity may occur. In four of the author's patients, multiple abscesses developed that were not complicated by fistula and empyema. These patients recovered, but follow-up roentgenograms showed persistent translucent areas that may have represented residual abscesses, sterilized by the employment of antibiotics. A long follow-up period will be required to determine what sequelae, if any, will occur.

Retrograde Aortography in the Diagnosis of Congenital Heart Disease in Infants. E. B. Singleton, D. G. McNamara and D. A. Cooley. J. Pediat. 47:720-726 (Dec.) 1955 [St. Louis].

Of five infants between the ages of 25 days and 2 years with congenital heart disease, in whom retrograde aortography was performed with the aid of local anesthesia, one had patent ductus arteriosus, one coarctation of the aorta, one true truncus arteriosus, one ventricular septal defect, and one aortic stenosis. Sodium acetrizoate (Urokon Sodium) in doses of 1 cc. per kilogram of body weight was injected with the aid of a 19 gauge Lindemann's needle into the brachial artery, which had been exposed through a 2 cm. longitudinal incision after the skin and subcutaneous tissues had been infiltrated with 1% procaine hydrochloride solution. After the completion of the injection of the contrast medium, the arteriotomy incision was closed with silk suture. Although a continuous murmur was heard on one occasion in the patient with patent ductus arteriosus, it was not sufficiently typical to warrant exploration without a definite diagnosis being established; retrograde aorotography showed opacification of the pulmonary artery segment by the contrast medium with simultaneous visualization of the arch of the aorta, establishing the diagnosis of patent ductus arteriosus. Severe congestive failure made immediate surgical intervention mandatory in this infant. Even though the clinical diagnosis of coarctetion of the aorta was apparent in the second patient, the demonstration in the retrograde arteriogram of the area of coarctation distal to the origin of the left subclavian artery confirmed the diagnosis and facilitated the surgical procedure. Although the evidence of right ventricular hypertrophy and arterial unsaturation suggested truncus arteriosus in the third patient, it was impossible from the catheterization data definitely to exclude patent ductus arteriosus or septal defect. Retrograde aortography showed communication between the aorta and pulmonary circulation and angiocardiography established the diagnosis of truncus arteriosus. It was impossible to determine from the clinical data and electrocardiograms whether the fourth patient had an interventricular septal defect or patent ductus arteriosus. Retrograde aortograms showed a normal

aorta without opacification of the pulmonary circulation, thereby ruling out patent ductus arteriosus. Because of absence of pulsations in the peripheral arteries, a diagnosis of aortic stenosis was considered in the fifth patient, but an unusual type of coarctation of the aorta could not be excluded without aortography. The diagnosis of congenital cardiac malformations in infants is frequently difficult. The authors' five cases illustrate the usefulness of retrograde aortography in establishing or excluding the diagnosis of several types of malformation in which the clinical findings may be similar and in which accurate and prompt diagnosis is often essential in order to determine whether the abnormality is surgically correctable.

Nephrosis Treated by Malaria: Results in 65 Cases. D. Gairdner and P. G. Shute. Lancet **2**:946-950 (Nov. 5) 1955 [London, England].

It had been reported in 1952 by two authors independently that remissions of nephrosis could be induced by infecting the patient with malaria. Following these reports the Malaria Reference Laboratory supplied many hospitals with infected blood or mosquitoes for the purpose of inducing malaria in nephrotic patients. The malaria was of the benign tertian variety, except in two instances where a second bout of fever was desired, when quartan malaria was used. The authors report the results of malaria treatment in 65 patients, 10 of whom were studied by one of the authors and 55 of whom were treated by other physicians. Fifty-one of the 65 patients fulfilled the conventional criteria of "pure nephrosis," showing gross edema and proteinuria, hypoalbuminemia, and hypercholesteremia but no hypertension or sustained azotemia, and little or no hematuria. Most of the remaining 14 patients showed, in addition to the nephrotic picture, hypertension, azotemia, and nephritis. Fourteen of the 51 with "pure nephrosis" achieved remissions lasting longer than three months, and 12 have remained well subsequently, with follow-up periods of up to six years. No lengthy remission occurred among the 14 patients with nephritic nephrosis. The only common complication of malaria treatment was anemia, which sometimes necessitated blood transfusion. One death was partly ascribable to malaria. The authors conclude that nephrosis is a long and disabling illness, carrying still a considerable mortality. While its etiology remains obscure, only empirical treatments exist. Among these malaria has a place, since long-lasting remissions can be induced in about one in four patients with "pure nephrosis," sometimes after hormone treatment has failed.

"Home Dyspepsia" and Treatment with Oxytetracycline (Terramycin). G. Schaper. Medizinische, No. 46, pp. 1601-1605 (Nov. 12) 1955 (In German) [Stuttgart, Germany].

Enteritis frequently develops in infants several days after their admission to a hospital or a nursing home, or it may appear in infants on their return to their home soon after discharge from a hospital or a nursing home. The term "home, or institutional, dyspepsia" instead of the previously used less descriptive term of "initial dyspepsia" is suggested for this type of enteritis to emphasize the fact that this disease is associated with the patient's sojourn in a children's hospital or a similar institution. This "home or institutional dyspepsia" is one of the various forms of manifestation of exogenic damage to which infants are exposed in a hospital or a nursing home. Two hundred five infants with this type of dyspepsia, of whom 51 were premature infants between the ages of 1 and 3 months and 154 were suckling infants between the ages of 1 and 4 months, were treated with oxytetracycline (Terramycin) at the pediatric clinic of the University of Münster in Westphalia, Germany. The antibiotic was given orally in doses of 50 mg. four to five times a day. A dose of 25 mg. four to five times per day proved to be equally effective. Treatment was continued for four days and the drug was well tolerated. The therapeutic effect of the drug became apparent within the first 36 hours; vomiting stopped simultaneously with a drop in temperature, which had risen up to 40 C (104 F). Increase in weight began after two days of treatment. Comparison of results obtained with oxytetracycline in the author's patients with those in 150 infants with home or institutional dyspepsia treated with change in diet, parenteral fluid administration, and sulfonamides showed that a greater number of infants treated with oxytetracycline than of controls gained weight and that the increase in weight was more considerable in the infants treated with oxytetracycline. Only one (0.5%) of the 205 infants died in the course of the oxytetracycline therapy. Treatment with oxytetracycline can be carried out without any dietetic measures and is well tolerated by young infants. Besides shortened duration of the treatment, the antibiotic makes it possible to give food of full qualitative value to premature and young suckling infants.

A Complex of Congenital Cardiac Anomalies: Ventricular Septal Defect, Biventricular Origin of the Pulmonary Trunk and Subaortic Stenosis. L. M. Becu, W. N. Tauxe, J. W. DuShane and J. E. Edwards. Am. Heart J. **50**:901-911 (Dec.) 1955 [St. Louis].

Four cases of a complex of congenital cardiac anomalies, consisting of a ventricular septal defect in conjunction with biventricular origin of the pulmonary trunk and subaortic stenosis, are described in infants who died 3, 7, 8, and 38 days after birth. Autopsies revealed that the ventricular septal defect did not involve the membranous portion of the ventricular septum but lay anterior to it and above the papillary muscle of the conus. When viewed from the right ventricle, the defect was seen to open into the distal portion of the outflow tract of the right ventricle. A dividing muscular ridge, which lay across the outflow tract of the left ventricle and encroached on the width of the subaortic portion of this outflow tract, was interpreted as the left extremity of the crista supraventricularis; it may have been the cause of the subaortic stenosis. The pulmonary artery was not transposed and was overriding the ventricular septal defect. The large size of the pulmonary trunk and the relative hypoplasia of the ascending aorta, which were common to all four patients, might be explained by the possible existence of the following hemodynamic features in the fetus. The pulmonary trunk overriding the outflow tract of the left ventricle coupled with the subaortic stenosis creates the possibility of a left-to-right shunt at the ventricular level during fetal life. Such a shunt conceivably could reduce the amount of blood that would flow through the ascending aorta and proportionately increase the amount of blood that would flow through the pulmonary trunk. Under these circumstances, it is possible for the pulmonary trunk to dilate and override progressively to a still greater degree the outflow tract of the left ventricle. The association of serious obstructive lesions of the aorta in the form of either coarctation or complete interruption of the aortic arch, in addition to the intracardiac malformations, appears to be particularly disadvantageous for extrauterine life. Early infantile death from pulmonary hemorrhage and edema occurred in the authors' patients. Since preparation of this paper one of the authors examined the heart specimen of a fifth infant who had died at the age of two weeks. The intracardiac defects in this case were identical to those in the four other cases. Significant malformations likewise were present in the aortic-arch system.

Corticotropin Therapy in Nephrosis. M. J. H. Frederikse. Maandschr. kindergeneesk. **23**:349-355 (Oct.) 1955 (In Dutch) [Leyden, Netherlands].

At the children's hospital with which the author is connected, 28 courses of corticotropin therapy were given to eight children (six boys and two girls) with nephrosis. The ages ranged between 2 and 11 years. Two of the children had been ill for a long time when treatment with corticotropin was begun, but in the six others corticotropin was given from the onset. A small amount of sodium in the diet of these children is advocated to prevent hyponatremia. Various corticotropin preparations were employed, and for this reason the doses varied, and some of the preparations were given in a single daily dose, whereas others were subdivided into several doses. Sixty per cent of the courses of corticotropin therapy proved very effective, 25% proved moderately effective, and 15% produced poor results. The dosage per kilogram of body weight varied and the courses usually lasted from 8 to 10 days. The author gained the impression that low doses accounted for the therapeutic failures. Symptoms of the nephrosis generally recurred after cessation of treatment, but at the time when this report was prepared

three children had been free from edema for over six months; they had normal erythrocyte sedimentation rates, and their urine was free from protein. The other five children are still receiving treatment.

UROLOGY

Hyaluronidase and Renal Calculi in Poliomyelitis. J. R. Taylor, A. J. W. Alcock and J. A. Hildes. Am. J. M. Sc. **230**:536-540 (Nov.) 1955 [Philadelphia].

To assess the value of hyaluronidase treatment in the prevention of new or additional renal stone formation, the authors made studies on 52 patients with poliomyelitis who required respirator treatment. The interval between the onset of poliomyelitis and this study ranged from 2 to 21 months, with an over-all average of less than 8 months. Urine retention in this series of severely paralyzed patients was a common complication during the early stages of their poliomyelitis. The trial was conducted over a seven-month period. The presence of renal calculi, as well as changes in number, size, and position, was determined by roentgen-ray examination carried out at the beginning of and at regular intervals throughout the trial. Of the patients without stones at the beginning of the trial, 12 were treated with hyaluronidase injections daily and 22 served as controls. Stones developed in one of the treated and four of the untreated patients. Of 18 patients with stones at the beginning of the trial, 14 were treated with hyaluronidase. Of this group, nine showed an increase in size or number of stones or both. Two of four untreated control patients with preexisting stones showed an increase in size or number of stones, or both. Although it cannot be definitely stated that hyaluronidase had no effect on the patients treated, it seems unlikely that the treatment was of practical benefit.

Hemangioma of the Kidney: Report of Two Cases. C. Ferguson, G. Cameron and J. Carron. J. Urol. **74**:591-595 (Nov.) 1955 [Baltimore].

Two cases of hemangioma of the kidney, a rare pathological condition, are described in a 49-year-old man and in a 41-year-old man. Both patients had gross hematuria and flank and costovertebral angle tenderness. A left nephrectomy was performed in the first patient and a right nephrectomy in the second patient. Microscopic examination of the removed kidneys revealed that the pelvic lesions consisted of cavernous spaces, and the fan-like radiations were composed of red blood cell masses in tubules. The ureters were normal. Both patients made an uneventful recovery. Hemangioma of the kidney is a true vascular tumor and is usually cavernous in type. Hematuria is produced when the hemangioma ruptures into the pelvis of the kidney. When bleeding becomes massive and threatens life, surgical or x-ray treatment may be lifesaving. The possibility of bilateral renal hemangioma must be considered when planning surgical treatment. Neither of the authors' two patients has had bleeding from the remaining kidney. The two cases reported on bring the total number of cases to date to 77 since the entity was first described by Virchow in 1867.

Carcinoma of the Penis in a Man Circumcised in Infancy. A. J. Paquin Jr. and J. M. Pearce. J. Urol. **74**:626-627 (Nov.) 1955 [Baltimore].

An epidermoid carcinoma of the penis developed in a Jewish 49-year-old man who had been ritualistically and adequately circumcised during infancy. The patient denied any history of venereal disease or trauma. He had not married until he was 40 years of age. The patient had no genitourinary complaints and his general condition was otherwise excellent. The lesion was found 1 cm. below the coronal sulcus in the region previously occupied by the base of the prepuce. It was ovoid in shape, 5 mm. in its greatest length, and 3 mm. to 4 mm. wide. The surface was hard, without discharge, and covered with a grey heaped-up scale. The entire lesion was freely movable and unattached to the underlying fascia. There were no enlarged inguinal lymph nodes. The entire lesion was excised elliptically with a good margin. Microscopically the stratified squamous epithelium was thickened and the normal cell layers lost. The cells were disorganized and pleomorphic with numerous mitoses. Although much of this lesion appeared to be a carcinoma in situ, there were regions consisting of definitely invasive epidermoid carcinoma in which keratinizing islands of tumor cells lay in the corium beneath the more normal epithelium. This is the fourth case of carcinoma of the penis in a circumcised Jew to be reported.

Needle Biopsy of the Kidneys: Studies of Two Cases of Lower Nephron Nephrosis Due to Toxic Solvents. W. C. Casey and W. Woolf. California Med. **83**:353-359 (Nov.) 1955 [San Francisco].

The authors report on needle biopsies of the kidneys in two patients with acute toxic nephrosis caused by organic solvents. The first patient, a woman aged 46, had been well until four days prior to being hospitalized with complaints of upper abdominal pain, backache, nausea and vomiting, and fever. The patient had cleaned curtains with a cleaning fluid containing petroleum naphthas, and after that she had sprayed plants in the garden with an insecticide. This patient was thought to have either acute gastroenteritis or obstruction of the small intestine and was managed accordingly. On the sixth day of illness, only 50 cc. of bloody urine was passed in 12 hours. Cystoscopic examination and ureteral catheterization showed no urinary tract obstruction, and retrograde pyelograms were normal. Lavage of both renal pelves with saline solution was carried out and a small amount of dark brown liquid was obtained. A diagnosis of acute renal failure was made, and a needle biopsy of the right kidney was performed approximately 12 hours after the onset of oliguria. The patient remained oliguric for 12 days; nausea, vomiting, and diarrhea persisted. The blood urea nitrogen and creatinine rose to high levels. Diuresis began after 12 days of oliguria and progressed through polyuria to a normal urinary output. The second patient was a 62-year-old man who became oliguric two days after drinking 60 cc. of carbon tetrachloride while under the influence of alcohol. The period of oliguria was short, and by the fifth day the patient was excreting 1,500 cc. of urine. Needle biopsy of the kidney was performed on the 12th day of illness. Histological studies made on the biopsy material of the kidneys showed changes confined mainly to the epithelium of the proximal tubules. They confirmed the diagnosis of toxic nephrosis. The needle biopsy had no adverse effect on the course of the disease and caused no complications; however, the procedure had been carried out in animals before it was used in human subjects. The authors feel that needle biopsy of the kidneys may prove as informative and valuable as needle biopsies of the liver by aiding in the prognosis as well as in the diagnosis of various renal diseases.

Colloid Bodies in the Urine. H. J. Hillenbrand and J. Roesner. Ztschr. Urol. **48**:609-618 (No. 10) 1955 (In German) [Leipzig, Germany].

Three stages could be differentiated in the formation of experimental renal calculi in rats. During the first stage characteristic formed elements appeared, which are spherical, homogeneous, almost colorless, transparent bodies. Their size ranges between 5 and 20 μ in diameter. They represent a precipitated protein or a crystalloid-colloid. For this reason they are designated as colloid bodies. In the second stage the colloid bodies assume a radiating striation and are called spheroliths, which measure from 10 to 40 μ. The formed elements of the third stage of development are the so-called microliths with a diameter of from 30 to 150 μ. These have, in addition to the radiating striations, concentrical stratifications. The authors examined the urines of unselected hospital patients for colloid bodies, spheroliths, and microliths. To improve the visualization of these formed elements they utilized an opal-blue-phloxine-rhodamine solution. Microscopic studies were made on 1,782 stained urinary specimens, obtained from 697 patients, including 447 men, 207 women, and 43 children. Colloid bodies, spheroliths, or microliths were found in 45 men, 10 women, and 3 children. The 58 patients included 8 with renal calculi, 15 with other disorders of the urogenital apparatus, 11 with fractures and bone inflam-

mations, and 11 with brain lesions. Patients with urogenital, bone, or brain lesions have a tendency to form calculi. Nevertheless the appearance of colloid bodies in their urine is frequently only a temporary condition, and true concretions develop only in some of them. The authors conclude that the appearance of formed elements in the urine gives information about certain processes in the organism, which, under certain conditions, may lead to the formation of calculi.

Kidney Biopsy: A Review of 100 Successful Needle Biopsies. A. E. Parrish and J. S. Howe. A. M. A. Arch. Int. Med. **96**:712-716 (Dec.) 1955 [Chicago].

The authors selected 100 successful renal biopsies and compared the clinical and pathological impressions. These 100 biopsy specimens were taken from a total of 169 biopsy attempts, of which 131 yielded renal tissue. The biopsy specimens in 31 patients were disregarded, because they were unsatisfactory or because they were repeat biopsies. Specimens were obtained by means of a Turkel needle. They were formalin fixed, paraffin embedded, sectioned, and stained with hematoxylin and eosin and whatever other stains were necessary. Such sections measured 5 to 20 mm. in length and 1 mm. across and consisted mostly of cortex containing 10 to 40 glomeruli. Renal biopsies were considered adequate only if at least 10 glomeruli were present. These sections show the condition of the glomeruli, convoluted tubules, loop of Henle, interstitial tissue, arterioles, and of the small arteries of the cortex. Clinical diagnoses were arrived at by carefully evaluating the history, physical examination, and laboratory data, including the examination of the urinary sediment. Renal biopsy established the diagnosis in 52% of the patients studied when the clinical impression was incorrect; it confirmed the clinical impression in 39% of instances, and in 9% neither the pathologist nor the clinician could arrive at a definite diagnosis. Biopsy was of least help in acute glomerulonephritis, where the clinical impression was right 89% of the time. It was also of little value when the clinical picture was not clear but when renal disease was thought to exist. Similarly, when clinical evidence suggested acute pyelonephritis, renal biopsy was not confirmatory. Biopsy proved of considerable value in the diagnosis of intercapillary glomerulosclerosis, chronic glomerulonephritis, nephrosclerosis, and rare diseases of the kidney such as polycystic disease, amyloidosis, and metastatic carcinoma.

OPHTHALMOLOGY

Magnification: Practical Applications of the Principles of Magnification to the Problems of Subnormal Vision. D. M. Gordon and C. Ritter. A. M. A. Arch. Ophth. **54**:704-716 (Nov.) 1955 [Chicago].

Anyone who does not have sufficient vision to perform efficiently his daily home or work tasks with ordinary spectacle-glass correction may be considered a candidate for low-vision aids. Any lens (or combination of lenses) that, when used to view an object, creates the illusion of an increased dimension is a magnifier. Magnification is a function of plus lenses. The choice of a magnifying device is dependent on the specific purpose for which it is required. Important considerations in guiding selection are power, or magnifications; working distance; field of view, and depth of field. Each of these factors varies with the others, and each tends to modify the others. A brief description is given of the available low-vision aids such as spectacles with high reading additions of as much as 10 to 12 diopter or more, magnifying glasses with or without supporting devices and with or without built-in illumination, projection instruments that give magnification as much as 25 times, contact glasses with and without the use of other vision aids, telescopic lenses for distant and near vision, and microscopic lenses for near vision only. The simple use of a high plus lens will be adequate for an amazingly large number of patients. Persons with moderate visual loss are often best aided by simply bringing the reading material closer to their eyes. This takes advantage of the fact that the retinal image is magnified in direct proportion to the proximity within which the object is moved closer to the eye. Frequently the patient can be handled by a combination of a high plus lens and some type of magnifying device. In the application of magnifying devices, it is important to remember that, while the lens magnifies the size of the image of the object viewed, it does not magnify the scotoma. The device must render the retinal image larger than the scotoma. In the case of generalized retinal depression as in optic atrophy the stimulus provided by the magnifier must be great enough to stimulate the retina to see. It is in the latter group that intense light is extremely important. These patients require a more concentrated light than does the group with macular lesions. No low-vision patient with measurable Snellen vision should be written off as hopeless until he has been given a good trial with magnifying devices.

Relationship of Epidemic Keratoconjunctivitis to the Adenoidal-Pharyngeal-Conjunctival (APC) Virus Syndrome. H. L. Ormsby, A. M. C. Fowle and A. Cockeram. Canad. M. A. J. **73**:710-712 (Nov. 1) 1955 [Toronto, Canada].

Epidemic keratoconjunctivitis, reported previously in Ontario in 1951, was again seen in the Toronto area in the winter of 1954-1955. From seven of these patients, strains of virus were isolated in tissue cultures of HeLa cells or trypsinized monkey-kidney epithelium. The disease was reproduced in a human volunteer using fourth passage of virus in tissue culture. Some of these strains of virus have been shown to belong immunologically to the type 3 adenoidal-pharyngeal-conjunctival group of viruses. Convalescent serums from four patients with epidemic keratoconjunctivitis taken during the 1951 Windsor epidemic, and from one of the 1954 patients, had antibodies to the "Trim" virus of Jawetz. This virus, isolated in California in 1955 from a patient from the Orient with epidemic keratoconjunctivitis, is also an adenoidal-pharyngeal-conjunctival agent but differs immunologically from the six types previously described by Huebner and co-workers.

THERAPEUTICS

A New Drug in the Management of Obesity: A Preliminary Report. J. D. McNair. Am. Pract. & Digest Treat. **6**:1652-1653 (Nov.) 1955 [Philadelphia].

A tablet that contains 1 mg. of the alseroxylon fraction of Rauwolfia serpentina and 5 mg. of amphetamine sulfate was used by the author in the treatment of 11 overweight patients. All but one had normal blood pressure. The patients were placed on a diet allowing a daily caloric intake of from 1,000 to 1,200 calories and requested to keep a record of daily caloric food consumption. Combined Rauwolfia and amphetamine therapy was begun with one tablet before each meal. Dosage was adjusted according to the response obtained or the occurrence of side-effects. The patients were weighed and interviewed at one-week to two-week intervals. The author gained the impression that a combination of Rauwolfia and amphetamine is an effective and well-tolerated agent for appetite-suppression in the obese individual. It produced less side-effects than amphetamine alone. Its freedom from side-effects and its mood-elevating effect make it particularly suitable for the management of chronic obesity, where gradual weight loss is preferable to a sudden sharp loss in that the patient has the opportunity to establish a dietary routine. This helps overcome the tendency to slip back into old eating habits, with subsequent weight gain.

Clinical Trials of *p*-(Di-2-Chloroethylamino)-Phenylbutyric Acid (CB 1348) in Malignant Lymphoma. D. A. G. Galton, L. G. Israels, J. D. N. Nabarro and M. Till. Brit. M. J. **2**:1172-1176 (Nov. 12) 1955 [London, England].

Sixty-two patients with malignant lymphoma were treated with *p*-(di-2-chloroethylamino)-phenylbutyric acid (CB 1348), a water-soluble aromatic nitrogen mustard. Twenty-three patients had Hodgkin's disease, 11 reticulum-cell sarcoma, 12 lymphocytic lymphoma, 8 chronic lymphocytic leukemia, 6 follicular lymphoma, one mycosis fungoides, and one exfoliative erythroderma. The drug was usually given by mouth, but a few patients

received the sodium salt of CB 1348 intravenously, either alone or in addition to oral treatment. The orally given dose ranged from 2 to 20 mg. a day (0.03 to 0.34 mg. per kilogram of body weight). In most cases it was either 0.1 or 0.2 mg. per kilogram daily (6 or 12 mg. for a patient weighing approximately 140 lb. [63.5 kg.]). For intravenous use, the sodium salt was freshly made up in isotonic sodium bicarbonate; single doses varied from 10 to 70 mg. A course of treatment usually lasted 3 to 6 weeks, but CB 1348 was given daily for 8 to 16 weeks to 13 patients and for 6 to 12 months to 3 patients. Fifteen patients had two courses at intervals of from 3 to 27 months, two had three courses, and one had six courses. Administration of the drug was discontinued when satisfactory improvement had been obtained. In some cases treatment had to be terminated because of neutropenia and thrombocytopenia. If there was no response, treatment was usually continued for six weeks before it was concluded that the patient was resistant to the drug. Prolonged treatment was given when improvement was progressive and the blood picture offered no contraindications. Twenty-five patients received more than 0.5 gm. of CB 1348; the largest total dose was 1.93 gm. given in the course of 12 months' continuous treatment. Striking remissions were obtained in four patients with Hodgkin's disease, in seven with lymphocytic lymphoma, in four with chronic lymphocytic leukemia and in five with follicular lymphoma. CB 1348 therapy was relatively free from gastrointestinal side-effects and proved to be less damaging to hematopoietic tissue than cytotoxic agents hitherto available for the treatment of malignant lymphoma. CB 1348 may be safely used in routine therapy if simple precautions are taken to avoid damaging the bone marrow. The drug should not be used within four weeks of the end of a full course of irradiation therapy or chemotherapy. As the total dose approaches 6.5 mg. per kilogram of body weight, there is a real risk of causing irreversible bone-marrow damage. An average course at 0.2 mg. per kilogram of body weight per day might last four weeks (5.6 mg. per kilogram). If maintenance therapy is contemplated in patients who show slowly progressive improvement during the initial weeks of treatment, who tolerate the drug well, and whose blood picture remains stable, the maintenance dose should not exceed 0.1 mg. per kilogram per day and may well be kept at 0.03 mg. per kilogram. It is probable that short courses of treatment carry less risk than maintenance therapy. Continuous therapy may give an illusion of "maintenance" to a remission that would have proceeded without further treatment.

Recent Studies on Albomycin, a New Antibiotic. G. F. Gause. Brit. M. J. **2**:1177-1179 (Nov. 12) 1955 [London, England].

Results of laboratory and clinical investigations of albomycin, a new antibiotic prepared in the Soviet Union from Actinomyces subtropicus, are reported. This antibiotic strongly inhibits the growth of gram-positive cocci, chiefly pneumococcus and Micrococcus (Staphylococcus). It inhibits the growth of micrococci (staphylococci) resistant to other antibiotics including penicillin, streptomycin, the tetracyclines, and erythromycin. It is also effective against a number of gram-negative bacteria such as the coli-dysentery group of organisms and Friedländer's bacillus. Its action is about 10 times as strong as that of penicillin. Chemically, albomycin belongs to the class of metal-containing peptides. It does not contain free alpha-amino groups, the latter appearing only after hydrolysis. It appears to be a cyclopeptide. Chromatographic studies revealed that the hydrolysates of albomycin contain seven amino acids, six of which were identified with ornithine, serine, glutamic acid, alanine, glycine, and proline. Albomycin is pharmacologically inactive; intravenous injections of large doses in animals do not affect the heart, blood pressure, or respiration. It is devoid of cumulative toxicity and pyrogenic action, and no local reactions are observed when it is injected subcutaneously or intramuscularly in animals or man; large doses up to 50 million units per kilogram of body weight are well tolerated. It forms a reversible complex with the serum proteins, which facilitates its circulation in the body. No side-reactions were noted after intrathecal injections in children. Albomycin proved effective in the treatment of pneumonia, especially in young children; in the septic complications of dysentery and measles; and in meningitis caused by penicillin-resistant pneumococci. It has also been used in the treatment of peritonitis and other surgical infections and for penicillin-resistant prostatitis and gonococcal urethritis.

The Effects of Reserpine and Chlorpromazine on Gastric Secretion. B. J. Haverback, T. D. Stevenson, A. Sjoerdsma and L. L. Terry. Am. J. M. Sc. **230**:601-604 (Dec.) 1955 [Philadelphia].

The occurrence of abdominal cramps and diarrhea during reserpine administration and of constipation following the administration of chlorpromazine suggested that these drugs have an effect on the gastrointestinal tract. The authors studied the effects of reserpine on the gastric secretion in 12 patients. One of these had chronic duodenal ulcer, but the others had no signs of gastrointestinal disease. Following a 12-hour fast a stomach tube was positioned in the gastric antrum under fluoroscopic guidance. The fasting contents were evacuated and the gastric secretion aspirated continuously for three hours and 15 minutes by means of a mechanical suction pump. The volume of successive 15-minute specimens was measured, and the free acidity titrated. The drug was administered intravenously in five instances and orally in eight. When reserpine was given orally, a gastric study was performed prior to the administration of the drug and then repeated four to seven days after the drug was started. The effect of chlorpromazine was studied in seven patients. Except for one, who had a healed duodenal ulcer, the patients were free from gastrointestinal disease. Reserpine administered orally or intravenously was shown to increase the volume and free acidity of gastric secretion. Chlorpromazine reduced the volume of gastric secretion but did not significantly change the free acidity. Chlorpromazine would appear to be the tranquilizing agent of choice when stimulation of gastric secretion is contraindicated.

The Danger of Decomposed Paraldehyde. A. L. Agranat and W. H. D. Trubshaw. South African M. J. **29**:1021-1022 (Oct. 29) 1955 [Cape Town, South Africa].

Paraldehyde has been classed as a safe hypnotic and was extensively prescribed before the barbiturates came into use. It is still considered valuable in hepatic insufficiency, delirium tremens, and certain mental diseases. This sporadic use of paraldehyde may be a factor in its danger; it will deteriorate if allowed to stand on the shelf. When exposed to air and light (or even in the dark), it can be oxidized by atmospheric oxygen to acetic acid. It may appear unlikely that acetic acid would not immediately be recognized by its characteristic odor; but, as both paraldehyde and acetic acid have pungent odors, it is possible that this difference may not be noted. The authors present the histories of three patients who suffered serious lesions from the administration of deteriorated paraldehyde. The first patient, a man aged 31, in status asthmaticus, was given 6 dr. (22 cc.) of paraldehyde by rectum. During administration the patient complained of a severe burning pain. Within the next few hours the pain in the rectum and lower abdomen became excruciating. The patient then came under the care of the authors. An examination of the rectum revealed extensive caustic burns. Laparotomy revealed free fluid in the abdomen and extensive white patches of corrosion with several perforations of the distal half of the large intestine. A colostomy was performed. The patient's condition remained critical for about a fortnight, owing to toxic absorption from the sloughing areas in the large intestine and several severe intestinal hemorrhages. Improvement was gradual, and he was discharged after six weeks. Subsequently a barium enema revealed extensive fibrous contractions of the lower part of the large intestine. He remained in fair health for about two years. Then intestinal obstruction developed, and the patient died after an operation to relieve this obstruction. The two other patients also were given deteriorated paraldehyde by rectum and suffered caustic burns, which in turn caused intestinal perforations and strictures requiring surgical repair. The authors feel that it should be a fixed rule that paraldehyde should never be used when it has been standing on the shelf for any length of time. Any paraldehyde that has been prescribed for an individual patient and not used for him should always be discarded when the patient is discharged.

Treatment of Diabetic Coma with Thiamine Pyrophosphate. H. van Marken Lichtenbelt and E. Florijn. Acta med. scandinav. **152**:259-269 (No. 4) 1955 (In English) [Stockholm, Sweden].

The authors point out that earlier investigators (Markees and Meyer in 1949) had reported the effectiveness of the intravenous administration of thiamine pyrophosphate in diabetic coma. In attempting to explain the mode of action of this treatment, Markees and Meyer had stated that these results are accompanied by a decrease in the pathologically increased pyruvic acid content of the blood and by improved phosphorylation. The authors studied several questions that are posed by the use of thiamine pyrophosphate in the treatment of diabetic coma. They show that acetoacetic acid interferes seriously with the determination of pyruvic acid according to the method of Friedemann and Haugen, and they describe a simple method to eliminate this disturbing influence. They did not find that the pyruvic acid content in patients with diabetic acidosis was abnormally increased. The thiamine pyrophosphate content was usually slightly increased and the phosphorylation of thiamine was normal. Intravenously injected thiamine pyrophosphate is decomposed rapidly by the phosphatases (always present in the plasma); thiamine pyrophosphate had no favorable effect in the treatment of diabetic coma. A slight decrease of the thiamine pyrophosphate content ensues after prolonged insulin treatment of diabetic coma; it may be compensated by oral or parenteral administration of thiamine.

Treatment of Thromboses: New Possibilities: Preliminary Report. A. Augusto, A. C. Ferreira and N. Castro Barbosa. Rev. brasil. med. **12**:287-292 (May) 1955 (In Portuguese) [Rio de Janeiro, Brazil].

A new product that dissolves arterial and venous thrombi and reestablishes blood to normalcy, as seen by hemograms, is presented. It is a ferment from the latex of Ficus officinalis, a tree found in great abundance in Latin American countries, mainly in Brazil. The latex is destroyed by heat even if moderate. It is strongly antihelminthic and anticoagulant. The anticoagulant properties of the latex are due to a ferment that was recently isolated by the authors from the latex (and to which the name Ficitine was given). Experiments in vitro and in animals proved the effects of the ferment on blood clots and on blood. Some of the experiments included are as follows: 1. Total blood clots obtained by Quick's modified test and placed in test tubes with some drops of the ferment were dissolved in 30 minutes. Some drops of the ferment dropped in the center of blood clots on glass surfaces of 3 or 4 cm. dissolved the clot in a few minutes. Blood from dissolution of the clots, observed microscopically, showed normal erythrocytes. 2. An injection of 1 cc. of the pure ferment or of a 1:4 solution of the ferment in saline solution to guinea pigs was well tolerated by the animals, but contact of the substance with the tissues produced necrosis at the point at which the injection was made. 3. Two fragments of equal size of a blood clot were placed in two different hemolysis tubes, the one with four drops of the ferment in 2 cc. of saline solution and the other with four drops of heparin. Both tubes were left for two hours at 37 C in the incubator. The clot in the tube containing the ferment was entirely dissolved before two hours, whereas the clot in the tube containing heparin did not dissolve. 4. An intravenous injection of 1 cc. of a 1:4 ferment-saline solution to rabbits was well tolerated. This preliminary note is reported to invite collaboration of colleagues for confirmation of the results. Extraction of the active principle from the latex offers no difficulties and is easily performed according to the authors' technique, which is described in detail. It consists of (1) addition of one volume of latex to 5 volumes of alcohol, after which the resulting mixture is shaken and (2) filtration of the alcohol in the mixture through filtration papers and exposure of the precipitate on the paper and over a cloth for evaporation of alcohol. Immediately after evaporation, the precipitate, still humid, is collected in a glass with distilled water (the same original volume of the latex in two equal portions). The precipitate is diluted in the first portion of distilled water and filtered through a small piece of filtering paper, over which the second portion of distilled water is poured. The filtrate is a yellow liquid, which is kept in the ice box in a graduate glass. After a few days the filtrate forms a precipitate above which there is a transparent liquid, which is the product used for dissolution of blood clots. This liquid is separated from the precipitate by decanting, kept in the ice box in an emery glass, and used as necessary.

PATHOLOGY

Mycosis Fungoides Followed for Fourteen Years: The Case of Dr. W. B. Cannon. J. C. Aub, S. B. Wolbach, B. J. Kennedy and O. T. Bailey. A. M. A. Arch. Path. **60**:535-547 (Nov.) 1955 [Chicago].

The case of Dr. Walter B. Cannon, who in 1932 was found to have mycosis fungoides, is valuable, not because the course of the disease was exceptional from a clinical point of view but because the histological specimens obtained from repeated biopsies and at autopsy make it possible to study the progression of the lesions through exacerbations and remissions. Dr. Cannon was a pioneer in the use of the x-ray in physiological experimentation and during the period from 1897 through 1908 he underwent considerable exposure to unfiltered x-radiation, repeatedly suffering serious burns on his hands and to a lesser extent on his face and the upper part of his body. Itching of the skin and fiery red papular cutaneous lesions appeared on his back, chest, thighs, knees, and elbows in the summer of 1931, 23 years after he had stopped his exposure to x-rays. Biopsies of these lesions in the fall of 1932 showed mycosis fungoides, which continued with exacerbations and remissions until his death in 1945 from an intercurrent pulmonary infection. He remained actively at work throughout this period. Other neoplastic diseases—basal-cell carcinomas, an epidermoid carcinoma, and a temporary leukemia—appeared at various times during these 14 years, but the principal clinical problem was that presented by the mycosis fungoides. The course of this condition was marked by many interesting phenomena: (1) frequent spontaneous remissions, especially in the early stages; (2) the slow rise in the white blood cell count to 32,700 per cubic millimeter with a concomitant absolute increase in the lymphocytes to a peak of 90%; and (3) the development of bilateral facial paralysis and deafness, subsequently relieved by x-ray treatment. Dr. Cannon's scientific interest led to a continuous exploration of new agents that might improve his condition. Vitamins A and D were found to be beneficial and were constantly administered. X-ray therapy proved to be of palliative value on three separate occasions, chiefly for relief of itching. The proper management of x-ray therapy in a patient already suffering from the effects of x-irradiation presented a challenging problem. Part of the value of the pathological material lay in the fact that each biopsy specimen was taken at a time and from a site that made it possible to relate the known clinical appearance of the lesions with the histological evidence of progression or remission. Neither the suggestion that the giant cells found in mycosis fungoides are produced by fusion of reticular or connective-tissue cells nor the theory that they may be derived from immature reticulum cells was borne out by the findings in this case. Evidence was found, however, to indicate that they are probably derived directly from the endothelium of blood vessels. Study of the histological material suggests that mycosis fungoides should be regarded, not as a neoplasm, but as a reaction (to agents unknown) that, like other known premalignant processes, leads to the development of neoplastic properties in responsive cells.

Cell Types and Histologic Patterns in Carcinoma of the Lung: Observations on the Significance of Tumors Containing More Than One Type of Cell. C. T. Olcott. Am. J. Path. **31**:975-995 (Nov.-Dec.) 1955 [Ann Arbor, Mich.].

It is generally agreed that the histological picture in carcinoma of the lung varies widely, but there is no agreement about the significance of this variability. The author reports observations

on the histological slides from 234 patients with carcinoma of the lung on whom autopsy was done. The cells found in the carcinomas were of four types: large polygonal cells (type A), small round cells (type B), epidermoid cells (type C), and columnar cells (type D), the last mentioned including adenocarcinoma and terminal bronchiolar carcinoma. Tumors composed exclusively of one or another of these four types of cells were found in 65% of the patients; growths containing mixtures of two or three types of cells were found in the remaining 35%. The large polygonal cells appeared to merge with small round cells, especially when they were found at the periphery of a mass of cells that contained the smaller cells near their center. Furthermore, the large polygonal cells sometimes were found alone in metastases from a primary tumor that contained both large polygonal and small round cells. Hence the possibility was considered that the large polygonal cells might often be transformed into small round cells. In a number of instances, moreover, the large polygonal cells were found in close apposition to epidermoid columnar cells, or both, the findings suggesting that the large polygonal cells may also give rise to cells of epidermoid or columnar type. In view of the mixtures of cells found in a large proportion of the growths and the apparent differentiation of the large polygonal cells into cells of other types, it appears that carcinoma of the lung, though obviously presenting various histological pictures, should be regarded as a single entity.

Islet-Cell Tumor of the Pancreas with Hyperinsulinism: Failure of Surgical and Alloxan Treatment: Report of a Case. J. Fisher, J. A. Gius and R. G. Janes. A. M. A. Arch. Path. **60**:628-634 (Dec.) 1955 [Chicago].

The authors present the history of a 57-year-old man who was hospitalized for recurrent episodes of confusion, jerking movements of the body, profuse perspiration, and disorientation, all of which occurred in the early morning hours. The attacks had begun about three months before and had gradually increased in severity. After breakfast the symptoms disappeared. Hypoglycemia was suspected, and the patient was fasted for 24 hours. This produced a severe reaction manifested by bizarre shaking movements, excessive perspiration, and confusion. At this time the blood sugar was 50 mg. per 100 ml. Administration of dextrose intravenously relieved the reaction. Both medical and surgical treatment did not halt the progress of the disease. The tumor was not found on two successive abdominal explorations in which about 90% of the pancreas was removed. Other therapeutic measures, including a high-protein, low-carbohydrate diet and cortisone, gave only temporary relief. Alloxan also produced only a temporary elevation of blood sugar and caused local and general reactions. An alloxan injection of 150 mg. per kilogram of body weight was followed by shock, dyspnea, cyanosis, high temperature, jaundice, coma, and death. The exact cause of death is somewhat obscure. At autopsy a small islet-cell tumor was found deep within the remaining pancreatic tissue in close proximity to the common bile duct. There was no histological evidence of necrosis of the islet cells either of the normal pancreas or tumor that could be attributed to alloxan. Other visceral changes, including parenchymatous degeneration of the liver, adrenals, and kidneys, were considered to be due to shock and the postmortem state. Alloxan in the doses used appeared to have only a temporary inhibiting effect on insulin production by the functioning islet-cell tissue. There is reason to believe that alloxan in large doses may have toxic effects on other organs. At the present time the only sure method of controlling hyperinsulinism caused by a functioning islet-cell tumor is by the surgical removal of the tumor.

The Serum Colloidal Gold Test—an Aid to Diagnosis of Struma Lymphomatosa. P. Skirpan, A. Reich and G. Crile. Am. J. Clin. Path. **25**:1274-1278 (Nov.) 1955 [Baltimore].

The fact that in 1954 Cooke and Wilder had reported a "persistent abnormality" of the serum colloidal gold test in two patients having struma lymphomatosa suggested to the authors of this paper that abnormal blood chemistry might have pathognomonic significance. To evaluate this suggestion, serum colloidal gold tests were performed and plasma cholesterol levels were determined at the clinical laboratory of the Cleveland Clinic on a series of 143 persons, including 19 patients proved by needle biopsy to have struma lymphomatosa (primary thyroid failure with compensatory thyroid enlargement). The serum colloidal gold test used was a modification of the method of Maclagan, differing by the substitution of commercially prepared colloidal gold solution and the quantities of serum and barbital buffer constituting the dilutions. Proportionally smaller quantities of serum and barbital buffer were used to reduce the amount of colloidal gold solution necessary for the test to 1 ml. for each tube. The serum colloidal gold test was positive in 15 of 19 patients with proved struma lymphomatosa and seemed to be more sensitive than serum cholesterol determinations in establishing a diagnosis of primary thyroid failure with goiter.

Anatomicopathological Pictures of Main Organs in Artificial Hibernation: Histological Study. G. Brancadoro, F. Mazzeo and R. Cuocolo. Minerva chir. **10**:803-811 (Aug. 31) 1955 (In Italian) [Turin, Italy].

Hypothermia ranging from 18 C to 30 C was induced slowly with an hourly temperature drop of 2 C in four groups of animals. The four animals of the first group in which a body temperature of 18 C was reached died immediately after the induction of hypothermia, two from undetermined causes and two from ventricular fibrillation during the reheating phase. Of the four of the second group in which a body temperature of 24 C was reached, one died from cardiac arrest soon after such temperature was obtained. All those of the third and fourth groups in which body temperatures of 27 C and 30 C, respectively, were reached survived. Some of the animals that survived were killed soon after the hibernation was induced, others from 1 to 10 days later. Biopsy specimens of the splanchnic organs and the lungs were made. When the abdomen was opened, a marked increase in the abdominal tension was noted in all the animals, but it was especially pronounced in those in which a body temperature of 18 C had been reached. This increase was related to edema of the organs and increase in the volume of the spleen and, to a lesser degree, of the liver and to the presence of fluid free in the cavity. The diaphragm was distended and pushed upward, the mesenteric lymph nodes were increased in volume, and the renal capsules were soaked with serous fluid as were the fat tissue and the loose preperitoneal and retroperitoneal tissue. The intrathoracic organs were also distended, especially in the animals of the first and second groups. As to the histological findings, shortly after the hypothermia was induced they were pronounced in the animals of the first two groups, and by the 10th day they had become irreversible in those of the second group. They were less marked in the animals of the last two groups immediately after the hypothermia, but by the 10th day they had disappeared almost entirely. The authors conclude that it is dangerous to lower the body temperature to values below 27 C because the resulting anatomic lesions are almost always irreversible.

Metastasis of Cancer to Cancer: Report of a Case. L. A. Schneider. Am. J. Clin. Path. **25**:1288-1289 (Nov.) 1955 [Baltimore].

The author presents the case of a 60-year-old man who had a six months' history of pain on urination. One week before admission he passed clots in the urine. The only physical finding of note was a greatly enlarged, hard and fixed prostate gland. Suprapubic cystotomy was performed and biopsy revealed adenocarcinoma. The patient died 2 weeks later. At autopsy a growth was found in the atrophic left kidney, which proved to be a clear cell carcinoma. Irregularly distributed throughout the renal tumor were groups of cells similar to those of the prostatic cancer. The rarity of metastasis of cancer to cancer remains unexplained. In the majority of the previously reported cases, as in the one presented here, the host neoplasm was a renal clear-cell carcinoma. In the addendum the author mentions the recent report of a case of angiolipomyosarcoma of the kidney that was the site of metastasis from a bronchogenic carcinoma.

INDUSTRIAL MEDICINE

Industrial Lead Poisoning in Relation to Climate. D. O. Shiels. Australasian Ann. Med. 4:178-182 (Aug.) 1955 [Sydney, Australia].

Studies carried out in Melbourne revealed that there is a greater incidence of industrial lead poisoning in the colder than in the hotter months. The author also studied the relationship between the climate, as measured by the maximum annual temperature, and the fraction of the total of those subjects with urinary lead content equal to or greater than 0.3 mg. per liter who had lead poisoning. When the number of those who had lead poisoning was expressed as a fraction of those with urinary lead content of 0.3 mg. per liter or over, the fraction was 1.00 for those experiencing lead exposure in the hot climate and 0.622 for those in the temperate climate. In earlier studies the author had shown the importance of sweat as a means for the elimination of lead. One may assume that in a hot climate the daily excretion of fluid was of the order of one liter of urine and 2.5 to 3.0 liters of sweat per day. With 0.3 mg. per liter of lead in the urine and a like concentration in the sweat, the total daily excretion in fluids would be greater than 1 mg. of lead. In the temperate climate the daily excretion of fluid may be assumed to be of the order of 1.5 liters of urine and 0.5 liter of sweat. With a concentration of 0.3 mg. per liter of lead in the urine and a like concentration in the sweat, the total daily excretion in body fluids would be 0.6 mg. of lead. In the former case the blood, organs, and tissues of the body would be in contact with more than 1 mg. of lead per day and, in the latter, with 0.6 mg. of lead. There would thus be a greater chance of finding cases of lead poisoning among persons excreting 0.3 mg. per liter of urine in the hot climate than among those excreting 0.3 mg. per liter in the temperate climate. On the other hand, from a constant amount of lead absorbed daily, more would be excreted in body fluids in the hotter months than in the colder, so that there would be less storage in the tissues. There would therefore be less chance of lead poisoning developing in the summer than in the winter if the conditions of exposure were the same.

An Unusual Case of Grease Gun Injury. J. H. Noble and C. J. Thuss. Plast. & Reconstruct. Surg. 16:297-302 (Oct.) 1955 [Baltimore].

Lubricating grease and diesel fuel oils under pressures ranging from 1,000 to 7,000 lb. per square inch, as in the case of grease guns, may penetrate the skin from distances up to 8 or more inches. A grossly evident break in the skin is not necessarily produced, and yet a surprising quantity of grease can be injected in a brief instant. Opinions are not unanimous on the immediate treatment of these injuries. The patient whose history is presented here had been hit in the left eye region by lubrication grease from a high pressure grease gun. There was a small cut in the skin and it bled slightly. The immediate result of the injury was a slight laceration and marked swelling of the lids of the left eye. The patient then entered the Korean War evacuation chain. Various treatments including penicillin and sulfadiazine were given during the subsequent weeks. About 10 weeks had elapsed before the patient was admitted to the eye section of the surgical service of an army hospital. The lesion was excised three months after the accident. Healing was prompt. The authors point out that previous reports on grease gun injuries described injuries involving the hand and fingers. Because of the anatomy of the hand and particularly the fingers with their dense, relatively inelastic cover and terminal arterial supply, early gangrenous changes have been frequent and have motivated authors to recommend immediate adequate removal of injected lubricating grease or diesel fuel oil. On the basis of the course of the case involving the eyelids, it is felt that in grease gun injuries involving more readily distensible tissues with less precarious blood supply than the hands, surgical treatment other than drainage might better be postponed until subsidence of the initial acute inflammatory process to a time when the lesion closely resembles the paraffinoma.

RADIOLOGY

Pitfalls of Myelography. W. C. MacCarty Jr. and F. W. Lane Jr. Radiology 65:663-670 (Nov.) 1955 [Syracuse, N. Y.].

The authors reviewed 400 consecutive cases in which Pantopaque myelography had been done and 223 patients operated on. Ruptured intervertebral disk was by far the most common pathological condition, being present in 181 cases. Tumor of the spinal cord, meninges, or extradural tissues was present in 19 cases. Six patients had only hypertrophic changes causing myelographic abnormalities. Vascular anomalies, present in eight cases, consisted of epidural varices or enlarged veins encircling the spinal nerve roots, which were almost invariably mistakenly diagnosed as a ruptured disk on the myelogram. Under the heading miscellaneous were grouped four cases with such diagnoses as arachnoiditis, congenital anomalies, and trauma. In five of the operative cases no abnormality was discovered at operation. Of 181 patients operated on for protruded intervertebral disk, 26 had involvement of more than one vertebra. The protrusions occurred most often in the low lumbar region, L 4-5 and the lumbosacral interspaces. Of the 207 disks removed only one occurred in the thoracic region. Myelography was correct in 89.3% of the ruptured disks. The authors discuss the pitfalls of myelography so that they can be avoided. Pantopaque is the contrast medium most frequently employed, but, because of its low viscosity, it tends to separate into droplets, and it does not provide the complete filling necessary for recognition of small nonobstructing lesions. This defect can be partially corrected by turning the patient in the supine position and allowing the medium to pool in the normal thoracic curvature. Errors in the technique of the injection of the contrast medium, such as perforation of the meninges, may cause extravasation of cerebrospinal fluid into the subdural space with resultant partial collapse of the subarachnoid space. Extradural injection occasionally occurs when the needle is accidentally dislodged from the subarachnoid space before the oil is injected. Another error is inadequate examination; it is often limited to the lower portion of the lumbar subarachnoid space, or only the level clinically indicated is scrutinized. In multiple disk involvement the symptoms of the larger and more caudally placed disk may mask those of a second located more cephalad. Variation in the number of lumbar vertebrae and anomalies of sacralization of the last lumbar body occasionally lead to miscalculation of the level of a lesion. There are errors due to variations in size and shape of the subarachnoid space. Patients with a narrow subarachnoid space and a large quantity of epidural areolar tissue between the thecal sac and the vertebral canal offer great diagnostic difficulty. Anatomic variations in the shape of the cul-de-sac are responsible for missing a ruptured disk at the lumbosacral interspace. In patients who have had previous myelography, laminectomy, spinal anesthesia, or occasionally even diagnostic lumbar punctures, the interpretation of indentations of the opaque column becomes difficult. Adhesions and scarring will often produce defects that are hard to analyze. While major lesions can usually be diagnosed fluoroscopically, it should be a policy to take spot films of questionable areas at the time of fluoroscopy.

Planigraphy in the Differential Diagnosis of the Pulmonary Nodule with Particular Reference to the Notch Sign of Malignancy. L. G. Rigler and E. R. Heitzman. Radiology 65:692-702 (Nov.) 1955 [Syracuse, N. Y.].

In 1948 one of the authors, Rigler, first observed a curious irregularity, or, as it was then called, an umbilication, on the margin of a shadow in a lateral roentgenogram of the lung, in a case later proved to be an undifferentiated carcinoma. The authors reviewed all their cases of pulmonary disease found during the past five years in which planigraphic studies were made. The object was to determine the value of such studies in the differential diagnosis of the peripheral lung nodule and to evaluate the significance of this "notch" sign in the diagnosis of pulmonary carcinoma. There were available some 550 cases in which lesions in the lung were suspected and planigraphic studies had been undertaken. By planigraphy the authors mean body section roentgenography. They found 132 patients in whom

planigrams had been made to determine the nature of a peripheral nodule. They apply the term peripheral nodule to what is commonly miscalled a "coin" shadow but actually represents a spheroidal nodule in the lung. They investigated the planigraphic findings in their cases for size, shape, and location, to determine whether such data would be of value. They found that calcification, cavitation, and the notch or umbilication sign were the only signs of any real significance. Calcification is a clear indication of the nonmalignant character of a lesion. There was not a single patient with malignant growth among the 29 in whom the planigrams showed definite calcification and in the 9 in which calcification appeared to be somewhat equivocal. Cavitation could frequently be clearly demonstrated by planigraphy, when it was not clear in conventional films. It is strongly indicative of malignancy. Of the 18 cases with cavitation, only 13 were proved unequivocally. Eleven of these proved to be malignant, while two were granulomas. The other five patients were either not operated on or failed to return. The notching or umbilication of a border of a spheroidal nodule is a new sign, which is best seen in planigrams but occasionally is demonstrated also on conventional roentgenograms. It is highly indicative of malignancy. Of the 32 malignant growths proved histologically, 15 showed a definite notch sign and 5 a more equivocal one, while in the remaining 15 it was not demonstrated. It should be noted that this sign is present in metastases as well as in primary carcinoma of the lung. The absence of the notch sign is of little or no significance in the determination of the malignancy of a peripheral lung nodule.

Bronchogenic Carcinoma—a Five-Year Survey. J. W. McKay and M. N. Lougheed. Canad. M. A. J. **73**:815-818 (Nov. 15) 1955 [Toronto, Canada].

One hundred forty-five patients with primary pulmonary carcinoma were treated at the Montreal General Hospital in Canada between January, 1950, and December, 1954. There were 127 men and 18 women, a ratio of 7 to 1. The average age of the patients was 62 years. One hundred thirty-seven are dead and eight are living. According to pathological classification after autopsy, 53 had epidermoid carcinoma, 37 anaplastic carcinoma, 7 adenocarcinoma, 3 alveolar carcinoma, 15 unclassified carcinoma, and 30 were unconfirmed. Of the eight survivors, two are alive 12 months and four years, respectively, after pneumonectomy, and two 15 months and 12 months, respectively, after irradiation therapy. One treated by preoperative irradiation and by surgery is well three years after the operation. Only three of the eight patients appear to be cured. Prognosis is very poor in patients with primary pulmonary carcinoma, no matter what therapeutic procedure is used. Failures are due to the disease having spread beyond the treatable area by the time treatment can be undertaken. Indications for the use of radiotherapy are (1) to make localized but inoperable cases operable; (2) for definitive treatment of technically inoperable cases; and (3) for palliation, because atelectasis is resolved, superior vena cava syndromes are relieved and prevented, metastatic pain is relieved, effusions are controlled, and morale is improved. Radiotherapy offers definite palliative value in suitable cases and is an important adjunct to surgery in other selected cases. The curative tumor dose lies between 4,500 and 6,000 r in six to eight weeks; the palliative tumor dose lies between 3,000 and 4,500 r in six weeks.

Palliative Rotatory Irradiation in Inoperable Pulmonary Cancer. J. Thoms. Nord. med. **54**:1559-1561 (Oct. 13) 1955 (In Danish) [Stockholm, Sweden].

Of the 70 patients with advanced pulmonary cancer treated by rotatory irradiation from 1943 to 1953, 56 were men, 14, women; 56 were aged 50 or over. The symptomatic effect of the treatment was reduction or disappearance of cough in 36 cases, of sputum in 35 cases, of dyspnea in 31, and of pain in 20, with improvement of the general condition in 29. The roentgenologically demonstrable extent of the tumor was reduced in 32 cases. The average duration of survival was 7.6 months for all patients and 8.3 months for those with microscopically verified diagnosis. The maximum time of survival was 39 months. Four patients are still living. There was no relation between the histological type and radiosensitivity. The general condition was good rather than poor in the patients in whom roentgenologic disappearance or decrease of the tumor infiltration was established, which allowed application of a larger tumor dose. Greater palliative effect is attained when "curative" doses are aimed at also in the hopeless cases. Rotatory treatment was well borne.

The Reliability of Cholecystography. I. G. Wickbom and V. Rentzhog. Acta radiol. **44**:185-200 (Sept.) 1955 (In English) [Stockholm, Sweden].

The reliability of oral cholecystography was studied on 1,340 patients in whom cholecystographic observations were interpreted as abnormal and on whom surgical interventions were performed at the Serafimer Hospital, Stockholm, Sweden, between 1937 and 1948. Up to 1943 a Swedish proprietary preparation of iodophthalein sodium (Cholotrast) was used as contrast medium; during 1944 and 1945, iodophthalein sodium and a Swedish proprietary preparation of iodoalphionic acid (Bilitrast) were used alternately, and after 1945 iodoalphionic acid was used almost exclusively as contrast medium. The day before the examination the patient was given a fatty meal to empty the gallbladder, followed by a double dose of the medium (8 gm. of iodophthalein sodium or 6 gm. of iodoalphionic acid). The patient was then kept on a light diet, all fats being withheld. The roentgenologic examination was carried out the next morning after the patient had been given a large water enema. A preliminary roentgenogram using a 24 by 30 cm. film was first obtained to see whether the gallbladder was sufficiently filled. If so, additional roentgenograms were taken under fluoroscopic control with the patient erect, the gallbladder being compressed, and a small diaphragm employed. Whenever no filling was evident, or visualization was so poor that the presence or absence of stones was uncertain, the patient was questioned regarding his proper ingestion of the contrast medium and as to any subsequent vomiting or diarrhea. In the latter event, he was examined again the next day after administration of a further dose of the contrast medium and tincture of opium. Attempts were also made to eliminate every other source of error. Results showed that, whenever roentgenograms of the gallbladder indicate the presence of gallstones, either directly or indirectly as defects in its contrast-filled lumen, the evidence may be relied on completely. If there is any calcification in the walls of the gallbladder it may be difficult to distinguish this from lithiasis, but the difficulty seldom occurs in practice. Failure of the gallbladder to fill with the contrast medium is almost conclusive evidence that it is diseased. Extensive injury to the liver parenchyma must be excluded, and it must be remembered that incipient hepatitis may prevent the gallbladder from filling before any sign of jaundice has developed. Other sources of error are retention of the contrast medium in the stomach, pernicious anemia, and breast-feeding. Other abnormal conditions in the biliary passages, particularly tumors of the gallbladder, biliary ducts, or head of the pancreas, also may cause defective filling. Duodenal ulcer may occasionally have the same effect. If the filling is so poor that it is impossible to state definitely whether or not stones are present, the same consideration as in the cases with no filling is warranted. If the filling is poor, but sufficient to indicate or exclude lithiasis, it need not be considered abnormal. However, if iodoalphionic acid has been given, the poor filling may sometimes denote disease of the walls of the gallbladder. Iodoalphionic acid is more likely than iodophthalein sodium to lead to filling of the gallbladder, regardless of whether or not its walls are diseased. Consequently, there is a better chance of visualizing stones directly with the use of iodoalphionic acid. In 75% of the patients in whom the gallbladder failed to fill, the walls of the gallbladder were diseased. However, changes in the walls were present in only 25% of the patients in whom stones were observed in a contrast-filled gallbladder. Normal cholecystographic findings practically always exclude disease of the gallbladder, but exceptions may occur. Collections of cholesterol flakes may be present that can form stones. A strong clinical suggestion of gallbladder disease may, therefore, occasionally warrant surgical exploration, provided all other conditions are first carefully eliminated. Sodium iodipamide (Biligrafin), a new intravenous contrast medium, was not on the market before the authors' studies were completed. Although the authors

consider oral contrast mediums most suitable for routine examinations, it may sometimes be advantageous to carry out examinations with sodium iodipamide.

Percutaneous Splenoportography. E. Adlercreutz, B. L. Lindström and S. Schauman. Nord. med. **54:**1551-1556 (Oct. 13) 1955 (In Swedish) [Stockholm, Sweden].

Percutaneous splenoportography allows closer investigation of different disorders within the field of the portal circulation. The main scope of indication is cirrhosis of the liver, where the appearance of intrahepatic portal branches and the occurrence of collaterals give an insight into the extent of the cirrhotic process. The greatest diagnostic value of the method is in portal thrombosis, which previously could not be diagnosed without the aid of laparotomy. The method is also useful in prognosis; cases with marked collateral formation are prognostically more unfavorable than cases with few or no collaterals. Splenoportography is indispensable for the surgeon when it is necessary to determine whether or not an anastomosis is feasible or when the choice lies between different operative methods and for postoperative control of the function of the anastomosis. It is also indicated in certain affections of the pancreas and tumors in the liver and the upper part of abdomen, likewise in cases of vague gastrointestinal bleeding. Twelve splenoportographies in disorders of the liver and pancreas are reported.

PHYSIOLOGY

The Function of the Pituitary Stalk. G. W. Harris. Bull. Johns Hopkins Hosp. **97:**358-375 (Nov.) 1955 [Baltimore].

It is suggested that the pituitary stalk functions as a connecting link between the external environment and the central nervous system on the one hand, and the pituitary gland and its target organs on the other. Experiments in which the stalk is cut or in which lesions are placed in the tuber cinereum show that the activity of the neurohypophysis is entirely dependent on its connection with the hypothalamus, whereas that of the adenohypophysis is largely, but not completely, dependent on its connection with the nervous system. It is probable that the hypothalamus and pituitary stalk are responsible for regulating the changes in activity of the two lobes of the gland in accordance with the needs of the organism in an ever changing environment. The fact that the anterior pituitary shows the ability to function at a low level of activity after pituitary stalk section may be compared with the function of the adrenal cortex and thyroid gland after hypophysectomy. The adrenal cortex of the hypophysectomized animal still preserves sufficient output of adrenal steroids to maintain the life of the hypophysectomized animal as compared with that of the adrenalectomized animal. Similarly, the thyroid gland still accumulates iodine and secretes thyroid hormone to some extent after hypophysectomy. A low level of autonomous function seems to be inherent in the glandular tissue. If the pituitary stalk functions as a connecting link between the external environment and the endocrine system, it is pertinent to ask whether the mechanism functions in the fetus when the external environment is relatively constant. There are some data indicating that the hypothalamo-hypophysial system only undergoes full maturation after birth. There seems to be some similarity between the endocrine system of the fetus or newborn animal and that of the adult after the pituitary stalk has been sectioned.

Relationship of Factor Isolated from Erythrocytes to Formation of Thromboplastin. S. I. de Vries, H. K. Kettenborg and E. T. van der Pol. Nederl. tijdschr. geneesk. **99:**2967-2974 (Oct. 1) 1955 (In Dutch) [Haarlem, Netherlands].

The authors isolated a factor from erythrocytes that accelerates the conversion of prothrombin into thrombin, and in the thromboplastin generation test it can serve as a complete substitute for the thrombocytes. With regard to the capacity to form thromboplastin, this factor is identical with the "platelet factor 3" of Van Crefeld and Paulssen, but it differs from that factor in that a lipoid factor can be extracted from it that does not neutralize heparin. Furthermore, it has an inhibiting effect on hemolysis in vitro. The authors feel that the term "lipoid factor" is better than "platelet factor 3" for this erythrocytic substance.

Relationship of Prolonged Drainage of Bile Through Pancreatic Duct System to Pancreatitis. F. S. Cross, F. L. Raffucci, E. L. Brackney and O. H. Wangensteen. Proc. Soc. Exper. Biol. & Med. **99:**208-213 (Oct.) 1955 [Utica, N. Y.].

The role of reflux of bile into the pancreatic duct system in the etiology of acute hemorrhagic pancreatic necrosis has been a subject of intensive investigation. When sterile bile is injected into the pancreatic duct of experimental animals, under certain conditions, a fulminating hemorrhagic pancreatic necrosis results quite regularly. There is evidence that under other more physiological conditions the presence of bile in the pancreatic duct is harmless to the pancreas. The experiments reported here were designed to show the effect upon the pancreas of draining all of the bile secreted by the dog's liver through the pancreatic duct system over long periods of time. The entire flow of bile was successfully diverted through the pancreatic duct system into the intestine in 11 dogs. In eight of these dogs a significant degree of pancreatitis failed to develop even though the average observation period was more than 60 days, and in only one dog in the series did a full-blown acute pancreatic necrosis develop. The result of these experiments indicate that the presence of bile in the pancreatic duct system under physiological pressures is tolerated for long periods of time without any serious damage to the pancreas in most cases.

PUBLIC HEALTH

BCG Vaccination in Morocco. J. Gaud. Semaine hôp. Paris **31:**3557-3564 (Nov. 14) 1955 (In French) [Paris, France].

Between April, 1949, and May, 1951, 2.2 million children and young adults were tested with tuberculin in Morocco, and the one million who were not reactors were vaccinated against tuberculosis by the intradermal injection of 0.1 mg. of fresh BCG vaccine. This campaign was carried out under the auspices of the C. I. T. (Campagne International contre la Tuberculose), which was sponsored by UNICEF. Since 1952, a program of systematic revaccination every four years has been under way, in which 500,000 children have been tested and 270,000 vaccinated intradermally with lyophilized vaccine. The results of this campaign have been most encouraging. At the pilot station at Yacoub el Mansour, the tuberculous morbidity was reduced from 46 to 13 per thousand. It was hard to get figures for the country as a whole because of the lack of civil government, but a study of the mortality from tuberculosis in different age and ethnic groups suggested that BCG has played a large part in the reduction of that mortality. Efforts are currently being made to avoid the two biggest inconveniences of the method of vaccination described, which are an unsuitably large number of reactions in the form of suppurative adenitis and the necessity of two gatherings three days apart of a population subjected to vaccination.

Tuberculosis Survey in Belgium: Tuberculization of the School Population of a Brabantian Village, 1947-1955. A Jeurissen and Mrs. Jeurissen-Lauwers. Acta tuberc. belg. **46:**373-384 (Oct.) 1955 (In French) [Brussels, Belgium].

Tuberculin tests were performed on school children in a village near Brussels, Belgium, over a period of nine years. The age at which these persons become allergic was seen to have advanced during this period, as shown by the fact that 22% of the children born in 1939 had positive reactions, as compared with 13% of those born between 1940 and 1943, 11% of those born between 1944 and 1947, and 4% of those born in 1948. This recession in age of primary infection is a consequence of the reduction of contagiousness among tuberculous patients. Because of the delay, there has been a decrease in bone and meningeal localizations, forms that affect young children in particular. Lymphatic-pulmonary tuberculosis is also becoming rarer, since it has a predilection for children aged from 4 to 7 years. Unfortunately, the number of extrafamilial contacts has not been much affected. The authors observed 64 conversions of the skin reaction, mostly in patients who did not take proper care of themselves. None of the primary infections had serious consequences.

BOOK REVIEWS

Vitamins and Hormones: Advances in Research and Applications. Volume XIII. Edited by Robert S. Harris, Professor of Biochemistry of Nutrition, Massachusetts Institute of Technology, Cambridge, Mass., G. F. Marrian, Professor of Medical Chemistry, University of Edinburgh, Edinburgh, Scotland, and Kenneth V. Thimann, Professor of Plant Physiology, Harvard University, Cambridge, Mass. Cloth. $9. Pp. 382, with illustrations. Academic Press, Inc., 125 E. 23rd St., New York 10, 1955.

This volume gives positive indication that advances have been made in our knowledge of vitamins and hormones. Data are presented that demonstrate that antibody response can be inhibited in deficiency states. Animal work has shown that the essential fatty acids protect animals against x-irradiation injury, maintain capillary pressure in the subcutaneous vessels, are necessary for normal cholesterol transport and metabolism, and are required for successful pregnancy and lactation. The chapter discussing the biosynthesis of ascorbic acid indicates that new tools are available to study the problem and its relation to other physiological processes. Two chapters discuss the physiology and chemotherapeutic action of vitamin B_{12}. A brief chapter on the vitamin requirements of human beings is included. The conclusion seems to be that vitamins, including vitamin B_{12}, will correct metabolic disorders resulting from existing vitamin deficiencies. There is a fine presentation of the question of parasitic infections and nutrition. The problem is reevaluated, and it is concluded that there is a definite causal relationship, as well as a synergism, between parasitic infestation and malnutrition and ill health. One of the chapters on hormones indicates that it is possible to study the relations of hormones, enzymes, and cell division as a result of recent additions to our knowledge in the field of endocrinology. This confirms the idea that a basic understanding of hormone action is to be found at the enzyme level. The last chapter considers the possible mechanism of hormone action and gives a clear picture of what the present knowledge could mean in answering some of the questions that have been asked about each of the hormones discussed.

Obstetrical Anesthesia: Its Principles and Practice. By Bert B. Hershenson, M.D., Director of Anesthesia, Boston Lying-in Hospital, Boston. With foreword by Frederick C. Irving, M.D. Cloth. $9.50. Pp. 403, with 50 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1955.

The author has presented a survey of the principles underlying sound practice in obstetric anesthesia, including a description of the methods employed at the Boston Lying-in Hospital. This book is divided into 10 chapters that deal with historical background, reflex irritability, pain in labor, premedication, signs and stages of general anesthesia, respiratory and circulatory derangements, asphyxia neonatorum, selection of anesthetic agent and technique, and complications. An index is included. Bibliographic references appear at the end of each chapter and in some instances are extensive. Seventeen tables assist in clarification of the text. The author wisely discusses the psychological as well as the pharmacological management of patients, including the necessity for meticulous adherence to the basic principles of pharmacological therapeusis. The value of inhalation anesthesia is stressed. The brevity of the discussion of ethylene, as well as one reference quoted, suggest that the author may be unfamiliar with the safe method of application of that anesthetic in obstetrics, as well as the extensive and satisfactory results obtained with it. The use of apomorphine hydrochloride during labor is discussed in detail. The need for accurate and complete clinical records is stressed. The necessity of developing good professional judgment in order to assure safe anesthesia for both the gravid woman and her infant is emphasized. The impossibility of standardizing anesthesia to fit all patients is well considered. Revision of this volume should include correction of a number of typographical errors. The printing, binding, and illustrations are excellent. Every physician dealing with obstetric patients should find this volume a valuable addition to his library.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Progress in Neurology and Psychiatry: An Annual Review. Volume X. Edited by E. A. Spiegel, M.D., Professor and Head, Department of Experimental Neurology, Temple University School of Medicine, Philadelphia. Cloth. $10. Pp. 645. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 99 Great Russell St., London, W.C.1, England, 1955.

This is the 10th in the series of volumes on progress in neurology and psychiatry edited by Dr. E. A. Spiegel. The 70 or more contributors cover the literature of 1954 on practically all aspects of neurology and psychiatry, including neurosurgery and psychology. More than 14,000 papers were reviewed. On this basis, the volume can be said to be comprehensive. There is, however, a wide variation in the quality of the different chapters. Some authors have attempted to analyze critically the significant contributions of the year in their field of interest, while others have felt obligated to mention every publication without presenting or discussing the facts contained in the more important publications. The volume is of special value to all physicians and research workers in the field of neurology and psychiatry in that it gives a general picture of the publications in these fields; however, in certain aspects of these fields the reader may need to refer to the original publication to obtain an insight into the progress achieved.

The Mechanisms of Healing in Human Wounds: A Correlation of the Clinical and Tissue Factors Involved in the Healing of Human Surgical Wounds, Burns, Ulcers, and Donor Sites. By Shattuck W. Hartwell, M.D., Attending Surgeon, Hackley Hospital, Muskegon, Mich. Publication number 250, American Lecture Series, monograph in Bannerstone Division of American Lectures in Surgery. Edited by Michael E. DeBakey, M.D., Professor of Surgery, Baylor University College of Medicine, Houston, Texas, and R. Glen Spurling, M.D., Clinical Professor of Surgery, University of Louisville, Louisville, Ky. Cloth. $4.75. Pp. 166, with 44 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1955.

The author in his foreword says: "This description of the processes and factors involved in the healing of human wounds is offered to all physicians, surgeons and students. It is a practical concept of the healing processes which may be applied to a more complete understanding of human wounds and to the selection of proper techniques for the repair or treatment of wounds." This little monograph includes a short summary, an adequate bibliography, and an index. The author stresses the fact that too much attention has been given to the histological findings of wound healing in laboratory animals and too little to the histological findings in human wounds. He believes that the cellular findings regarding fibroplasia in human wounds, which heal by primary intention, give strong support to the concept that mononuclear cells, especially the lemmocytes, provide the substance found in the repair of all white, fibrous, connective tissue in wounds. The healing fibrous scar is related not only to the cellular and chemical factors present but also directly to physical forces that are constantly passing through the wounded area. The author repeatedly points out that in the healing of the epithelial layers of the human skin the process is different from that in most laboratory animals that have been used in studies of wound healing. He believes that the basal cell layer of surface epithelium is an adaptive layer of the more primitive epithelial layers and that all living layers of the epithelium take an active part in producing the healing of epithelium, which extends into the wound by an ameboid activity. The concept is ingenious and has much to commend it. This monograph is recommended to all those interested in wound healing.

QUERIES AND MINOR NOTES

VITAMIN B_{12}

To the Editor:—*What use has vitamin B_{12} other than in the treatment of pernicious anemia?*

Andrew A. Love, M.D., Burbank, Calif.

Answer.—Vitamin B_{12} (cyanocobalamin and its congeners), like most vitamins, is effective only in clinical conditions in which it replaces a deficiency. There is no evidence that it is more effective in "pharmacological" dosage like, for example, vitamin D in certain types of calcium deficiency or that it will produce toxic effects when given in unduly large amounts like vitamin A. In general, the therapeutic uses of vitamin B_{12} are precisely those established by clinical experience over many years for highly purified solutions of liver extract, which are in fact essentially solutions of vitamin B_{12}. The existence of vitamin B_{12} deficiency can readily be detected by a determination of the serum vitamin B_{12} level by microbiological methods. Using the growth of the chlorophyll-containing flagellate Euglena gracilis, the normal range of serum vitamin B_{12} is from 300 to 800 micromicrograms per cubic centimeter. Vitamin B_{12} is likely to be effective only in nutritional macrocytic anemias in which the serum vitamin B_{12} level is less than 100 micromicrograms per cubic centimeter: pernicious anemia including its neurological complication, the macrocytic anemia of fish tapeworm infestation, certain instances of the macrocytic anemia of pregnancy and of infancy, of tropical or of nontropical sprue, and of intestinal short circuits and stenoses. Because only certain bacteria and Streptomyces, and not higher plants, produce vitamin B_{12}, strict vegetarians or others with severe chronic dietary deprivation of animal protein, especially growing children, may also develop vitamin B_{12} deficiency. When dietary deficiency or intestinal disease is responsible for nutritional macrocytic anemia, it may be due to a deficiency of folic acid. In that case, despite indistinguishable blood and bone marrow morphology, vitamin B_{12} therapy will be ineffectual, while folic acid therapy will succeed. With or without significant anemia, combined system disease, the classic neurological complication of pernicious anemia, is associated with a low serum vitamin B_{12} level. It can always be arrested by vitamin B_{12} therapy, but a return to normal function of an irreversibly damaged nervous system may not be possible. There is theoretical reason to believe that vitamin B_{12} might be generally useful in growing children or other persons who are not receiving adequate natural sources of vitamin B_{12} in the form of milk or meat. As an actuality this is not yet well documented. Laboratory evidence indicates that vitamin B_{12} may have a lipotropic effect because of its influence on transmethylation reactions, a reducing effect on the SS group of certain sulfhydryl (SH) activated enzymes, as well as less clearly defined effects on carbohydrate and fat metabolism. A practical clinical demonstration of these actions of vitamin B_{12} has, however, not yet been made.

DIGITALIS PREPARATIONS

To the Editor:—*Kindly discuss whether digitoxin has a place in digitalis therapy.*

M.D., New Jersey.

Answer.—The administration of digitalis preparations has become, in the past few years, a controversial matter. For over 100 years digitalis was given more or less empirically and in a rather crude form. Absorption was uncertain, the dose was varied widely, and there was a great margin of safety between the therapeutic dose and the toxic dose. Within the past few years the physician finds himself presented with several different digitalis preparations—many of them pure principles—that have different absorption and excretion rates and different average doses, and there results a mounting number of cases of digitalis intoxication. This points clearly to the need for greater discrimination in the use of these preparations together with a more intimate knowledge of their characteristics. Practically all of the digitalis preparations (pure principles) in use in the United States today are represented by digitoxin, gitalin, digoxin, and lanatoside C. Any of these will be found effective in most patients, but they have different rates of absorption and excretion and the average single dose is different in each. If any one of these preparations is administered to a patient, not in a measured number of milligrams but to produce the desired clinical effect and with careful watching for signs of toxic reaction, it is quite likely that any of these drugs will prove satisfactory. The whole problem resolves itself into a need for a better understanding of the various preparations and the methods of obtaining a satisfactory clinical result without intoxication. Granting this, any of the pure principles may be used satisfactorily.

ELECTROSHOCK THERAPY

To the Editor:—*What are the limits of voltage and amperage employed by psychiatrists in shock therapy of mental patients? What is the frequency of use of electroshock therapy? Is the passage of electric current in itself, if the individual survives, productive of any ill-effects on the human body other than the destruction of tissue? Will any permanent ill-effects be produced on the heart of a 58-year-old man with early coronary heart disease after receiving an electrical shock (220 volts) that apparently produced only an ecchymotic area (36 sq. cm.) of the arm that cleared up spontaneously?*

M.D., Ohio.

Answer.—The voltage used in electroshock therapy varies from 120 to 450 volts (root-mean-square). The average current sufficient to produce a therapeutic convulsion varies from 20 to 500 ma., the necessary peak-to-peak current from 924 to 1,670 ma. The frequency varies from 28 to 120 per second. The passage of such currents through the brain under therapeutic conditions, that is when prolonged apnea and anoxia are avoided, ventricular fibrillation and other disturbances of the cardiac rhythm are prevented by adequate premedication with atropine, and if musculoskeletal complications are prevented by administration of succinylcholine chloride, does not cause destruction of tissues and usually is not productive of any ill-effects except for the following potential complications: (1) myocardial failure and/or infarction probably due to mechanical factors related to increased inflow load of the heart on release of the Valsalva phenomenon at the end of the therapeutic seizure, as well as due to vasoconstriction incidental to electroshock (the former of these two complicating factors is prevented by adequate premedication with succinylcholine chloride); (2) peripheral vascular collapse, possibly related to excessive vagal stimulation; (3) pulmonary edema; and (4) ventricular fibrillation and other disturbances of the heart rhythm, including cardiac arrest, also caused by vagal stimulation. The latter can be prevented by medication with atropine. While ventricular fibrillation is the most dangerous physical complication of electroshock, it is relatively rare if the shock is administered through cranial electrodes such as used in electroshock therapy, provided the body of the patient is not otherwise grounded while the machine itself is adequately insulated so that accidental grounding of the patient's body is rendered impossible. Ventricular fibrillation, however, is indeed a frequent and regular complication of accidental electroshocks that pass through the heart itself. Ventricular fibrillation occurs most consistently with shocks at amperages between 90 and 900 ma., provided that the electricity flows during the phase of the heart action represented by the T wave of the electrocardiogram. The likelihood of production of ventricular fibrillation decreases with shocks above 900 ma.,

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

while with shocks of 25 amp. and above, ventricular fibrillation can no longer be produced. Shocks with 25 amp. and above can even be utilized to bring about resuscitation of a patient whose heart is fibrillating due to a shock received with lower amperage (countershock). The facts that most household currents are within the fibrillation-inducing range and that one contact is usually a hand or an arm are responsible for the relatively high rate of fatalities with electrical accidents in the household.

As to the specific case, obviously a case of accidental electrical injury, permanent ill-effects can be produced on the heart of a 58-year-old man with early coronary heart disease after receiving an electrical shock (220 volts) that apparently produced only an ecchymotic area of 36 sq. cm. on the arm that cleared up spontaneously. In this case it must be assumed that the current flowed through the heart region, since one of the areas of contact was one of the arms. Assuming that resistance at the time of contact was 5,000 ohms, it can be assumed that in the course of a fraction of one second of contact his resistance declined to 1,500 ohms, thus allowing flow of a current of about 147 ma. Such a current is well capable of producing ventricular fibrillation as well as vasoconstriction of the arteries of the heart, provided that the current was flowing through the heart region. There is no doubt that such an episode of vasoconstriction as well as of disturbed activity of the heart muscle (fibrillation) can aggravate existing coronary disease. Increased work of the heart, interference with coronary artery filling, as well as vasoconstriction incidental to an electric shock through the heart region, may alone or together aggravate preexisting coronary heart disease. In ventricular fibrillation there is little or no coronary artery filling; this together with vasoconstriction would contribute to myocardial ischemia, particularly in the presence of preexisting coronary artery disease. Vascular collapse also would contribute to myocardial ischemia.

BURNING SENSATION IN SCROTUM

To the Editor:—*A 58-year-old white man is in good health except for an annoying burning of the scrotum that he claims is internal. Examination reveals nothing. Five years ago, a transurethral resection was done because of benign hypertrophy. His postoperative course was complicated by an acute epididymitis. I have used nicotinic acid, estrogens, and antihistamines with discouraging results. Have you any suggestions?* *Arthur F. Schiff, M.D., Miami, Fla.*

Answer.—It would be well in a case of this type to have a neurological and neurosurgical consultation to exclude the possibility of a cauda equina lesion that might be causing the unusual burning in the scrotum. In most cases symptoms of this kind are of a psychosomatic nature and, except for the application of heat, little can be done. The application of anesthetic ointments or the injection of novocaine into the scrotum usually provides only temporary benefit. Reassurance that there is no malignant disease present often does as much for the patient as anything else. Suggest that the patient try hot sitz baths several times weekly after neurological abnormality has been excluded.

DEPIGMENTATION OF THE FACE

To the Editor:—*I have occasion to see areas of depigmentation on the face both in the winter and summer. These are definitely not fungus according to scrapings. How might I be certain that I am not overlooking a vitiligo? I always examine the patients to see if they have any other areas.* *M.D., Alabama.*

Answer.—Vitiligo is seen most frequently on the hands, then the face. The patches are completely depigmented and tend to increase slowly both in number and size. A comon cause of partial depigmentation of the face is erythema streptogenes (Dobes, W. L., and Jones, J.: Erythema Streptogenes, *Arch. Dermat. & Syph.* **53**:107-114 [Feb.] 1946). The disorder is seen on the cheeks, forehead, and other parts of the faces of children and is more prominent in Negroes because of the color contrast. Streptococci or micrococci (staphylococci) can usually be cultured. The lesions respond to prolonged treatment with tar or ammoniated mercury.

TREATMENT OF CARBUNCLE

To the Editor:—*What is the best treatment of acute carbuncle to prevent spread and to prevent recurrence?* *William S. Levy, M.D., Woonsocket, R. I.*

Answer.—The necrotizing infection of skin and subcutaneous tissue called carbuncle is usually due to Micrococcus (Staphylococcus) aureus. Penicillin is ordinarily the antibiotic of choice for initial use, but cultures should be made to determine sensitivity since resistant organisms are increasingly common. Intramuscular injection of at least 300,000 units of procaine penicillin twice daily should be used to prevent metastatic infection but cannot be solely relied on to control the carbuncle. Local injection of aqueous penicillin into the subcutaneous tissue outside the indurated periphery of the carbuncle has been successful in quickly controlling spread of the carbuncle and resolving it with a minimum of tissue necrosis. A dose of 100,000 units of crystalline penicillin dissolved in 5 cc. of saline solution to which is added 5 cc. of 2% procaine hydrochloride produces a solution containing 100,000 units of penicillin per cubic centimeter. A dose of 4 to 6 cc. is placed about the periphery by four needle punctures, laying down a line about the lesion. It should not be placed into the carbuncle. A daily injection for one to five days is indicated until beginning peripheral resolution occurs. Meanwhile, general body rest and continuous warm, wet compresses to the area are important. Central sinuses must be opened to allow drainage, and necrotic tissue must be débrided as it appears. Wide cruciate incisions may often be avoided by this method but may be indicated for some carbuncles. X-ray therapy has proved of less value. Spread is prevented by the local penicillin injections about the periphery of the lesion and metastatic spread by parenteral therapy. Phisoderm may be applied to the surrounding skin twice daily. Recurrent micrococcic infections may be due to repeated or continual skin traumas allowing bacterial entry, to excessive oiliness or moisture that disturbs the protective outer layer of the skin, to decreased resistance secondary to uncleanliness, or to malnutrition or emotional stresses, or they may be secondary to metabolic disease such as diabetes. The organisms may be resistant to the antibiotic being used. Reinfection may be carried from the outer vestibule of the nose via the hands. Swabs of that area should be cultured and an appropriate antibiotic used in the nasal area. Neomycin ointment may prove effective there if organisms are resistant to other drugs. Autogenetic vaccine is occasionally useful, although, in general, its use has been disappointing.

DISABILITY FOLLOWING REMOVAL OF ACOUSTIC NEUROMA

To the Editor:—*Following the removal of an acoustic neuroma in 1948, a patient has not been able to return to private practice. He has tried to maintain an active interest in medicine and is working at a hospital on the study of headache. I would appreciate correspondence with someone who is in charge of vocational rehabilitation of individuals with this type of disability.* *M.D., Massachusetts.*

Answer.—The disabilities that result from the removal of an acoustic neuroma are of various types. Partial or complete deafness on the operated side is frequent, but this is usually a minor handicap. Of more importance are the symptoms resulting from compression or injury to the neighboring structures adjacent to the tumor. Among these is facial paralysis due to a lesion of the seventh cranial nerve. The palsy is conspicuous and thus may interfere with the normal life of a doctor. Correction by plastic surgery is helpful in some instances. Even more serious is the anesthesia of the side of the face and cornea occasioned by injury to the fifth or trigeminal nerve. Corneal ulceration may follow, requiring supervision by an ophthalmologist. The "anesthetic" lips allow food to collect unnoticed, resulting in annoyance and an unsightly appearance at meals. If the motor branch of the trigeminal nerve has been destroyed, there is some weakness of chewing, but this does not present much of a disability if the normal side is intact. Thirdly, there is the ataxia associated with cerebellar deficit leading to difficulty in using the hand in writing and in performing complicated movements, such as giving an intravenous injection. If the leg is involved, there

may be uncertainty of gait, with ataxia and difficulty in walking. Finally, there is the psychological effect of a severe intercranial operation on individuals who find it difficult to readjust to bodily handicaps. This is particularly true when it happens to physicians who have started in practice and now find they can no longer continue their work. Not every patient would have all the above symptoms, but, if enough of them are present, there is indeed a problem in regard to vocational rehabilitation. Many of the symptoms are fixed and, although not progressive, are irreversible. The patient must arrange to meet his disability on a permanent basis. This may preclude the continuation of previous practice or even hospital training. The usual method is to turn to some modified field of medicine, such as part-time association with a laboratory or a center for vocational rehabilitation. The psychological disturbance, if present, should be handled by a competent medical advisor, either a psychiatrist or a practitioner versed in this field. Something can be done by retraining to overcome the ataxia. The patient may learn to write with his left hand and use this hand for many maneuvers usually carried out by the right. If the tumor has been completely removed, and particularly if it was nonmalignant, a good deal of satisfaction should be gained from the knowledge that the disease in all probability is not a recurrent one.

PARASITES IN PIGEONS

To the Editor:—*I would like information concerning pigeons as a health hazard. Can pigeons on the outside of a child's room shed any parasites or other noxious products that might cause a skin rash?*

M.D., Virginia.

Answer.—Pigeons carry the viruses of Newcastle disease and ornithosis (psittacosis), as well as Salmonella organisms, none of which would be responsible for a human rash. Pigeons occasionally suffer from Erysipelothrix rhusiopathiae infection (swine erysipelas), which might cause a rash in man, but the probability of such infection under the conditions mentioned are remote. The fowl mite, Dermanyssus gallinae, is a ubiquitous parasite that causes a rash in man, but the probabilities of infection from a pigeon are not great.

ECZEMA AT ONSET OF MENSTRUATION

To the Editor:—*A woman, aged 24, developed severe eczema of the hands, face, and legs with the onset of menses at the age of 10. The rash breaks out violently about two days before each menstrual period and lasts for about two weeks. It then heals, and she is asymptomatic until the cycle is repeated with the next period. During her pregnancy eight years ago, she was free of the rash for the entire nine months. Numerous dermatologists have made a diagnosis only of eczema. She was considered at a dermatological conference some time ago, and an oophorectomy was advised in an attempt to control her symptoms. I am reluctant to do oophorectomy on a patient who has no demonstrable pathology in the pelvis and wonder if endocrinological studies might not be of value.*

R. M. Shepard Jr., M.D., Tulsa, Okla.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Not infrequently, annoying symptoms and distressing conditions that begin before the onset of menstruation can be relieved by the therapy used to prevent the symptoms of premenstrual tension. One theory of the etiology of premenstrual tension is insufficiency in the amount of progesterone secretion before menstruation. Mazer and Israel (Diagnosis and Treatment of Menstrual Disorders and Sterility, ed. 3, New York, Paul B. Hoeber, Inc., 1951) have had excellent results with progesterone therapy in cases of premenstrual tension. In pregnancy there is greatly increased progesterone production, and this may be a reason that this patient was free from eczema during her pregnancy. Hence, progesterone should be tried in this patient during the premenstrual period. The dose is 10 mg. every second day from day 14 to 24 of the menstrual cycle. After three or four months' treatment, some women have long-lasting relief. Greenhill and Freed (*J. A. M. A.* 117:504 [Aug. 16] 1941) believe that premenstrual distress is the result of sodium ion retention by the different tissues in the body under the influence of the ovarian steroids. This retention of sodium is associated with an increase in extracellular fluid in the tissues. Patients with premenstrual tension are advised to refrain from adding table salt to their food during the last two weeks of the menstrual cycle. During this time they are given 0.6 gm. of ammonium chloride three times daily. A large number of women have been treated with this simple remedy, and nearly all of them have been relieved of premenstrual distress. Another simple and effective agent is testosterone propionate. The patient may be given 25 mg. hypodermically on the 10th and the 3rd day before the expected menstruation, or better still, she can take a 10 mg. tablet of methyltestosterone orally or a 5 mg. tablet sublingually daily for 10 days before the expected onset of menstrual flow (Freed, S. C.: *J. A. M. A.* 127:377 [Feb. 17] 1945).

Answer.—This condition well may be considered as a bizarre manifestation of premenstrual tension. Usually, the symptoms found in the premenstrual phase are subjective, consisting of irritability, anxiety, depression, and general emotional instability. The objective signs are usually bloating of the abdomen, edema, and tender breasts, but occasionally other changes are found including alterations of the skin. These are usually acne, but lesions around the mouth; urticaria; and pruritus, especially around the vulva and the anus, have been observed. It would seem that the removal of the ovaries would be a most drastic procedure to combat the physiological causation of premenstrual changes. Certainly, the patient should be given a trial with the ordinary medication used for premenstrual tension. It is suggested that 25 mg. of testosterone propionate be injected six to seven days before the expected menses. If this is not completely effective, supplemental therapy with reserpine or chlorpromazine may be administered, since recent reports indicate that usefulness in this condition.

TRICHINOSIS

To the Editor:—*Is there a practical and safe method for meat inspection for trichinosis as a control of Trichinella spiralis infestation in slaughter and meat distribution centers?*

M.D., California.

Answer.—The only method for inspection of meat for Trichinella spiralis, the organism causing trichinosis in the human being, is a microscopic examination of every piece of pork processed. Since this is obviously impractical, the Bureau of Animal Industry has issued specific instructions on how pork products are to be handled so as to render them safe for human consumption. This agency has conducted extensive experiments to determine the lethal effects of temperature, refrigeration, curing, and drying that are necessary for the destruction of the parasites. The parasites are easily destroyed by heat, being killed at a temperature of 55 C in a few minutes. Pork can also be rendered safe for human consumption by proper refrigeration. The critical temperature is about −12 C. At this temperature the Trichinella organisms are killed in relatively short periods of time. There should be no danger of trichinosis, therefore, from any pork-containing products that are obtained from federally inspected packing houses.

GALACTOSEMIA

To the Editor:—*A 6-month-old child who has galactosemia is doing nicely on a milk-free diet. Is it ever advisable to give lactose in the diet? If so, at what age should one add milk?*

M.D., Tennessee.

Answer.—Lactose after being ingested is hydrolyzed in the intestinal tract into glucose and galactose. Galactose is not metabolized in the tissues but is metabolized in the liver to glycogen. In some normal infants saturation of the normal liver metabolism occurs, so that galactose may spill over into the urine. This is only temporary. In chronic galactosuria and galactosemia there is a congenital defect in galactose metabolism in the liver. In such cases the defect seems to be permanent and a milk-free diet is necessary for the remainder of life. Only

minimal amounts of milk or lactose in other foods are tolerated. Because of this congenital error in metabolism a milk-free diet is necessary. The only guides one has are hepatomegaly, galactosemia, galactosuria, and the galactose tolerance tests. The sequelae of hepatomegaly with cirrhosis, jaundice, cataracts, stunted growth, and mental retardation occur when milk is fed. Although these changes are more or less reversible in early infancy, they may not be so later.

CORONARY INSUFFICIENCY

To the Editor:—*A 39-year-old physician, three years ago, had a squeezing retrosternal pain occurring with maximum exertion, such as running during a tennis match, but not with long walking or climbing stairs or other less severe and intense exertion. The pain subsided in one-half to one minute after cessation of activity. The general physical examination, the electrocardiogram, chest x-ray, ballistocardiogram, blood cell count, sedimentation rate, and serologic tests were normal. Three years ago he was advised to continue with his usual activity but to refrain from severe exertion. In the three years since the first occurrence of this symptom, there have been no symptoms referable to the coronary arteries. The examination at present shows no abnormality. The patient would like now to resume his favorite sport, tennis. What would you recommend?* *M.D., California.*

Answer.—Not infrequently symptoms of coronary insufficiency with effort may be the only evidence of coronary heart disease. If this be slight, angina pectoris will appear only with unusual exertion or excitement. Coronary disease with or without myocardial infarction is far from rare in males under age 40. One would be particularly suspicious in the case referred to if the patient is of muscular body build, has a strong family history of coronary heart disease, has a dietary history of high-fat intake and increasing obesity, shows an elevated serum cholesterol level, shows evidence of mild diabetes by glucose tolerance test, or has significant changes in the electrocardiogram during an exercise test. It is likely that he will benefit from moderate exercise, providing that this does not cause a reappearance of symptoms, but it would be wise for him to continue to avoid severe exertion.

SWEET AND SOUR CREAM

To the Editor:—*Kindly advise as to the chemical difference between sour cream and sweet cream. Can butter be made from sour cream, and, if so, how?* *M.D., New York.*

Answer.—No chemical difference other than acidity is known between sour cream and sweet cream. Sour cream is defined as cream whose acidity is more than 0.20%, expressed as lactic acid. Either sweet cream or sour cream may be used for the manufacturing of butter. There is no difference in the process of manufacture of butter from either sweet cream or sour cream.

TRAUMA AND CANCER

To the Editor:—*On Jan. 22, 1955, a 112-lb. (50.8 kg.) 50-year-old, para 1, white female fell while carrying a load of groceries in her right arm. She incurred a mild contusion of the right breast. On July 20 she noted a small lump in the same area, which, when removed, measured 3 by 2 cm. A pathological report described it as a mammary duct carcinoma, grade 3, with metastasis to one midaxillary lymph node. The patient's history and her physical examination are negative. Please advise as to the latest findings on the question of trauma and cancer. Names of investigators in this field, particularly those who have favorably considered trauma as a predisposing factor, will be appreciated.* *V. Lentini, M.D., Downey, Ill.*

Answer.—There is no evidence that a single episode of trauma can produce cancer in any organ. There have been, however, several reports where the relationship of repeated trauma may have caused cancer, particularly sarcoma (Pack, G. T.: The Relation of Cancer to Trauma, *Compensation Med.* **3**:5, 1950; Pack, G. T., and Bocher, R. J.: Localization of Metastatic Cancer by Trauma, *New York J. Med.* **49**:1839, 1949; and Saphir, O.; Appel, M., and Levinthal, D. H.: Attempt to Localize Tumor Metastasis in Long Bones by Mechanical Trauma, *Cancer Res.* **5**:722, 1945).

ARTIFICIAL PNEUMOPERITONEUM

To the Editor:—*I understand many institutions have discontinued the use of pneumoperitoneum in treatment of pulmonary tuberculosis and rely on chemotherapy and surgery. Are there any physiological changes that indicate its value or is its use merely mechanical?* *M.D., Pennsylvania.*

Answer.—The use of artificial pneumoperitoneum in the treatment of pulmonary tuberculosis varies greatly in different parts of the world. It is still used quite extensively in many places, but in others, particularly in this country, it has given way largely to antimicrobial drugs and resectional surgery; however, it is still used in exceptional cases. Its use is mechanical in elevating and reducing the activity of the diaphragm, thus relaxing the lungs.

TYPHOID CARRIERS

To the Editor:—*In* The Journal, *Oct. 29, 1955, page 979, is a reply regarding procedure in the diagnosis of typhoid carriers. It may be well to recall that typhoid bacilli may be carried in the urine as well as in the feces. In releasing a patient convalescing from typhoid fever, it is recommended that three negative cultures of feces and urine be obtained at least 24 hours apart and not earlier than one month after onset. Occasionally a pure urinary carrier of typhoid will be found. In this type of carrier, the stool may be consistently negative and the carrier condition will be missed unless the urine is also cultured.*

James R. Enright, M.D.
Department of Health
Honolulu, Hawaii.

PROTHROMBIN DETERMINATION

To the Editor:—*In Queries and Minor Notes in* The Journal, *Aug. 27, 1955, page 1576, the reply to the query on a practical procedure for home prothrombin determinations is incomplete. Since 1944, I have used a simple blood prothrombin test for the control of anticoagulant therapy. Exhibits of this test and the results were shown at the American Medical Association Annual Meeting in Los Angeles, 1954; the Interim Session in Miami, Fla., December, 1954; and again at the A. M. A. Annual Meeting in Atlantic City, N. J., June, 1955. I have used this method in more than 1,200 subjects and found it practical. It has made anticoagulant therapy available to patients at home and in communities where more adequate laboratory facilities are not available. It is accurate and reproducible and has been taught to more than 200 physicians. My experience with this procedure was published in* Circulation, *November, 1954. Another article will be published in the December issue of* Postgraduate Medicine.

Benjamin Manchester, M.D.
3200 16th St., N.W.
Washington 10, D. C.

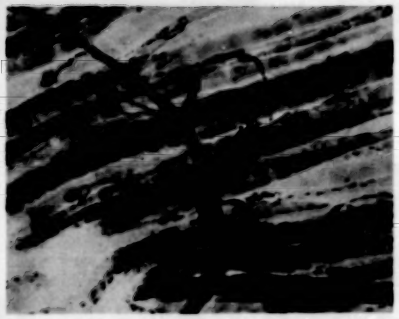
To the Editor:—*In Queries and Minor Notes in* The Journal, *Aug. 27, 1955, page 1576, a questioner asked if a reliable bedside prothrombin test was available and the answer stated there was none. I would like to call attention to the method developed by Dr. Benjamin Manchester of Washington, D. C., and demonstrated at the American Medical Association Clinical Meetings of 1954 and 1955, and published in* Circulation (**10**:691 [Nov.] 1954). *In my experience in a general hospital where control methods and comparison studies were made, this test is a practical and reliable means of regulating anticoagulant therapy.*

James C. Bruce, M.D.
1029 Madison Ave.
Greensboro, N. C.

THE MANAGEMENT OF ACUTE POLIOMYELITIS

USE OF RELAXOTHERAPY, HYPERPROTEINIZATION AND OTHER FORMS OF SUPPORTIVE THERAPY

GEORGE J. BOINES, M.D. WILMINGTON, DELAWARE



MUSCLE NERVE PHOTOMICROGRAPH

Showing Portion of Tensed Fragment of Rat Muscle

Photograph by Dr. George J. Boines from slides prepared by Dr. Mac V. Edds, Jr.

Since 1941, we have made several modifications to the Sister Kenny regimen, believing them to be improvements. Chief among these was the gradual substitution of carefully measured injections of curare (Tubadil) for hot packs, to the point that hot packs are no longer used. As adjuvant therapy, we use whole blood and intravenous fluids to combat dehydration, fever, and anemia; an oxygen tent where indicated for hypoxia or anoxia; Vitamins C and P (Hesper-C) to correct capillary fragility, high protein diet (Vi-Protinal) to overcome muscle catabolism; analgesics for nerve root pain; and a tranquillizing drug (Dimethylane) to combat tension—all with appropriate physical and occupational therapy and psychologic rehabilitation. Studies begun in 1954 indicate that intramuscular trypsin (Parenzyme) may be valuable in reversing the inflammatory reaction of the spinal cord and thus halting the paralytic process. With these measures we have seen a gratifying recovery rate and have been able to reduce hospital time to about one-third that of 1941.

PATHOPHYSIOLOGIC CHANGES IN ACUTE POLIOMYELITIS

These can be

RELIEVED . . . CORRECTED . . . PREVENTED

by POSITIVE THERAPY

SYMPTOMATIC . . . PSYCHOLOGIC . . . REHABILITATIVE

1- Early diagnosis and early treatment	→	1- Immediate hospitalization
2- Toxicity and weakness due to uremia, dehydration and fever, anemia	→	2- SUPPORTIVE IV fluids, whole blood
3- Anoxia and hypoxia in C.N.S. and muscular system	→	3- Oxygen tent
4- Muscle pain, spasm, stiffness, weakness or paralysis	→	4- Respiratory, tubocurarine°-assisted exercises, physical and occupational therapy, hydrotherapy, supportive mechanical aids
5- Increased capillary fragility and permeability, sludging of the blood, edema and inflammatory change of CNS, hemorrhages in cord and brain	→	5- Vitamins P and C°°, intramuscular trypsin°°°
6- Increased protein catabolism with loss of muscle tissue	→	6- High protein diet and protein supplements°°°, adrenal cortical extract
7- Nerve root pain	→	7- Analgesics, NO NARCOTICS
8- Respiratory muscle paralysis, paralysis with obstruction of pharynx, larynx and airway	→	8- Respiratory, tubocurarine°, curarae, tank respirator, rocking bed, aspiration, tracheostomy
9- Emotional dysfunction	→	9- Psychologic rehabilitation

Pain and stiffness are due to muscle spasm
Relieve with RELAXOTHERAPY and exercise Curare is NOT a cure
It permits ACTIVE therapy and earlier ambulation

° TUBADIL
°° HESPER-C
°°° PARENZYME INTRAMUSCULAR
°°°° Vi-PROTINAL

POSITIVE THERAPY . . . HASTENS RECOVERY PREVENTS COMPLICATIONS

Most **DEFORMITIES** · · { • are caused by muscle spasm • are not prevented or corrected by braces

MUSCLE SHORTENING and **ANKYLOSIS** may result from { • painful muscle spasm • prolonged immobilization • inadequate physiotherapy

Excessive **ATROPHY** may result from { • prolonged immobilization • poor circulation • poor nutrition

CONTRACTURES . . . MAY BE CAUSED BY FAILURE TO ESTABLISH EARLY MAXIMAL RANGE OF JOINT MOTION

MECHANICAL AIDS . . . ensure early mobilization . . . and are discarded when muscle strength and balance are regained

Presence of spasm may be easily seen in this acute stage of poliomyelitis, as evidenced by these photos of various muscle groups.

Neck, Back and Hamstrings

Neck, Back, Hamstrings and Gastrocs. Note pained "tripod" position.

Left quadratus lumborum pulls left lower extremity, producing apparent shortening.

Tensor fascia lata muscle.

Hamstrings—note shortening.

In spasm of neck, child is unable to touch chest with chin without opening mouth.

Posterior neck muscle in spasm.

Quadriceps, gluteus medius and tensor fascia lata muscles in spasm.

Elbow flexion caused by spasm in both brachialis muscles. Triceps normal.

Characteristic "foot drop" caused by spasm in gastroc soleus muscles.

Spasm in pectorals.

Spasm in elbow flexors, and complete paralysis of triceps.

POSITIVE THERAPY . . . HASTENS RECOVERY PREVENTS COMPLICATIONS

Most **DEFORMITIES** . . { • are caused by muscle spasm
• are not prevented or corrected by braces

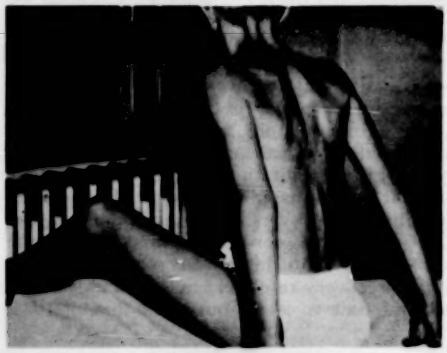
MUSCLE SHORTENING and **ANKYLOSIS** may result from { • painful muscle spasm
• prolonged immobilization
• inadequate physiotherapy

Excessive **ATROPHY** may result from { • prolonged immobilization
• poor circulation
• poor nutrition

CONTRACTURES . . . MAY BE CAUSED BY FAILURE TO ESTABLISH EARLY MAXIMAL RANGE OF JOINT MOTION

MECHANICAL AIDS . . . ensure early mobilization . . . and are discarded when muscle strength and balance are regained

Presence of spasm may be easily seen in this acute stage of poliomyelitis, as evidenced by these photos of various muscle groups.



Neck, Back and Hamstrings

Neck, Back, Hamstrings and Gastrocs. Note pained "tripod" position.

Left quadratus lumborum pulls left lower extremity, producing apparent shortening.

Tensor fascia lata muscle.

Hamstrings—note shortening.

In spasm of neck, child is unable to touch chest with chin without opening mouth.

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CLINICAL EXPERIENCES IN 664 POLIOMYELITIS PATIENTS

CLINICAL EXPERIENCE IN 190 PATIENTS AT WILMINGTON GENERAL HOSPITAL WITH HEMIMOBILIZATION... PACKS... NEOSTIGMINE... and NEOSTIGMINE + PACKS

RELAXOTHERAPY

CURARE *... PROTEIN - CARBOHYDRATE - VITAMIN SUPPLEMENTS **... VITAMINS P+C ***... INTRAMUSCULAR TRYPSIN ****

464 PATIENTS AT WILMINGTON GENERAL HOSPITAL - DORIS MEMORIAL UNIT

	1941	1942-1946	1947 to 1954 Average 60 pts/yr	1954 to 1955 1 year
NO. OF PATIENTS	19	171	464	60
TREATMENTS	HEMIMOBILIZATION	PACKS, NEOSTIGMINE NEOSTIGMINE + PACKS	RELAXOTHERAPY* PLUS NUTRITIONAL SUPPLEMENTS	RELAXOTHERAPY - CURARE* + NUTRITIONAL SUPPLEMENTS** + VITAMINS P+C*** + INTRAMUSCULAR TRYPSIN****
NON-PARALYTIC AVERAGE HOSPITAL DAYS	10 25.6	70 28.6	170 18.3	7 11.1
SPINAL PARALYTIC AVERAGE HOSPITAL DAYS	9 [illegible]	70 71.3	175 32.1	39 36.1
BULBAR PARALYTIC AVERAGE HOSPITAL DAYS	0 0	33 48.2	89 35.7	15 23.3
EXPIRED	1	10 [illegible]	16	3 [illegible] 4%

NOTE: Marked drop in hospitalization days with RELAXOTHERAPY

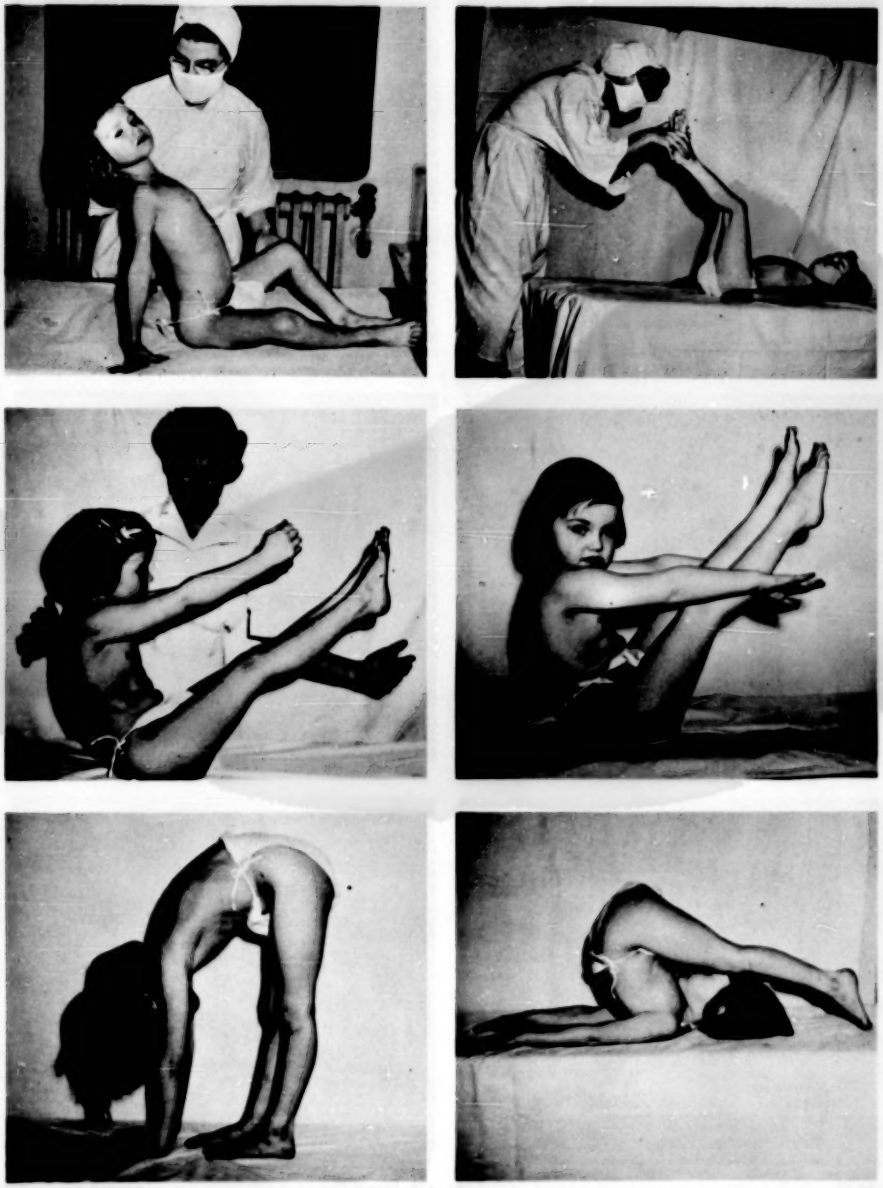
	Without Relaxotherapy or Nutritional Supplements	With RELAXOTHERAPY + NUTRITIONAL SUPPLEMENTS
SPINAL PARALYTIC	71.3	36.1
BULBAR PARALYTIC	48.2	23.3
NON-PARALYTIC	28.6	11.1

RELAXOTHERAPY:

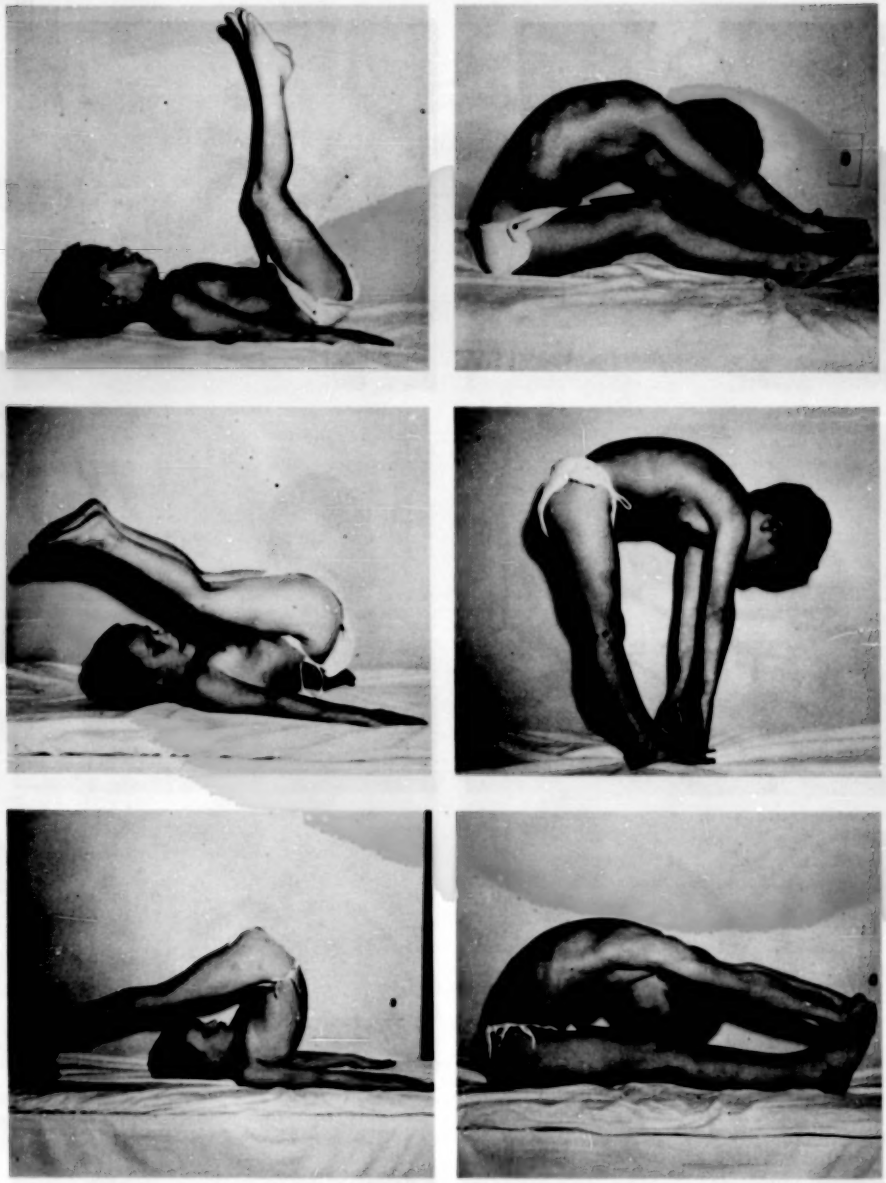
- * TUBOCURARINE (Tubadil) • Resistive Exercises
- ** HYPERPROTEINIZATION (Hi-Protinol)
- *** VITAMINS P+C (Ninger-C)
- **** ANTI-INFLAMMATORY THERAPY (Pancreatic Intramuscular Trypsin)

Before injection of Tubadil (curare in oil) one daily IM injection of one tenth (0.1) cc. per ten pounds of body weight.

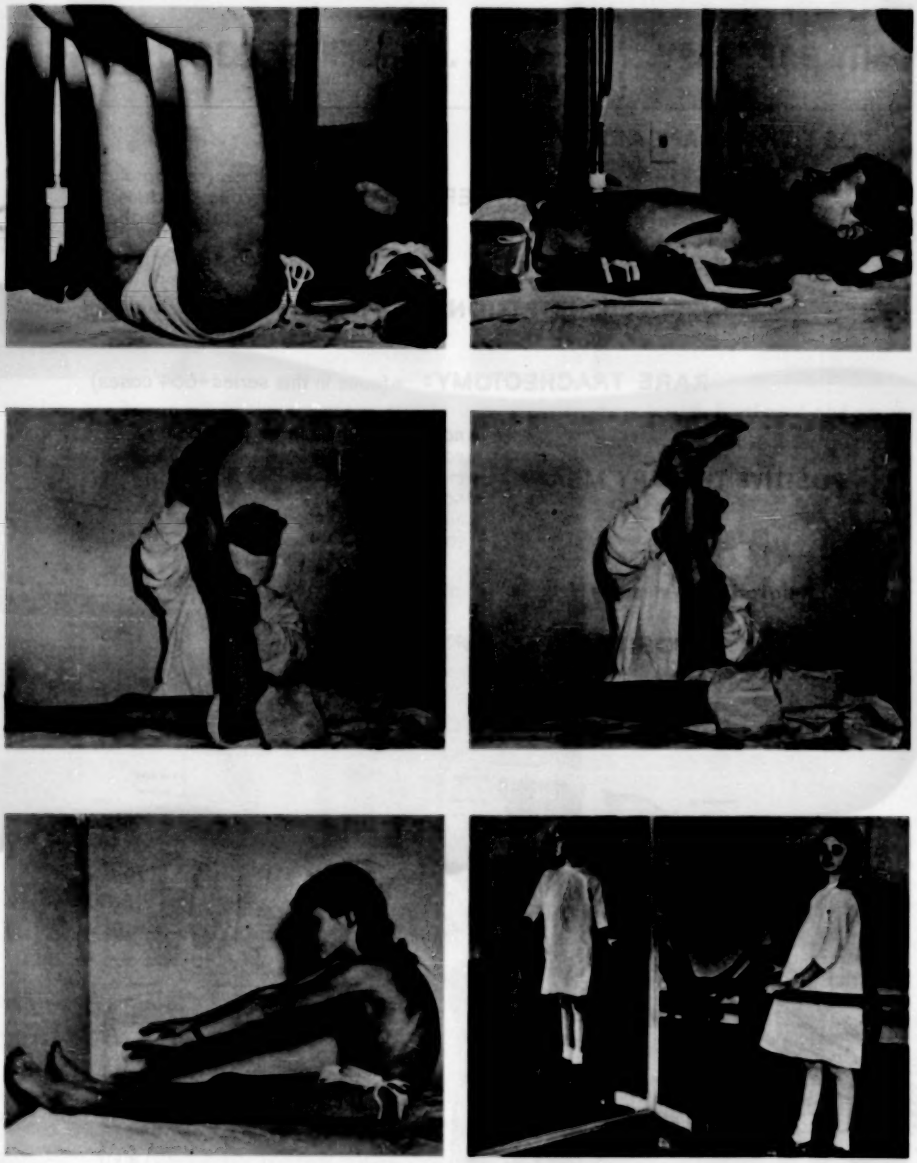
Thirty minutes after injection. Note expected signs of eyelid ptosis, listlessness, and functional denervation of neck muscles.



Under curare therapy, with adjunct measures, the acutely paralyzed patient (top) is able to exercise painlessly, preventing atrophy and progressing to recovery with full range of motion in all joints (bottom). Duration of therapy: six weeks.



In another case, Relaxotherapy permitted an acutely paralyzed boy (top) to immediately begin exercises for reeducation and coordination of muscles, progressing to full recovery as shown.



In this case, with nuchal rigidity and paralysis of both lower extremities, stretching exercises were followed by functional rehabilitation (lower right). Last photo taken 12 weeks after institution of therapy.

POSITIVE THERAPY.. {RELIEVES / CORRECTS / PREVENTS} .. PATHOPHYSIOLOGIC CHANGES

POSITIVE THERAPY ACHIEVES

EARLIER:
- mobilization
- ambulation
- hospital discharge (non-paralytic - 12 days) (paralytic - 33 days)
- maximal functional restoration
- normal activities
- socio-psychologic adjustment

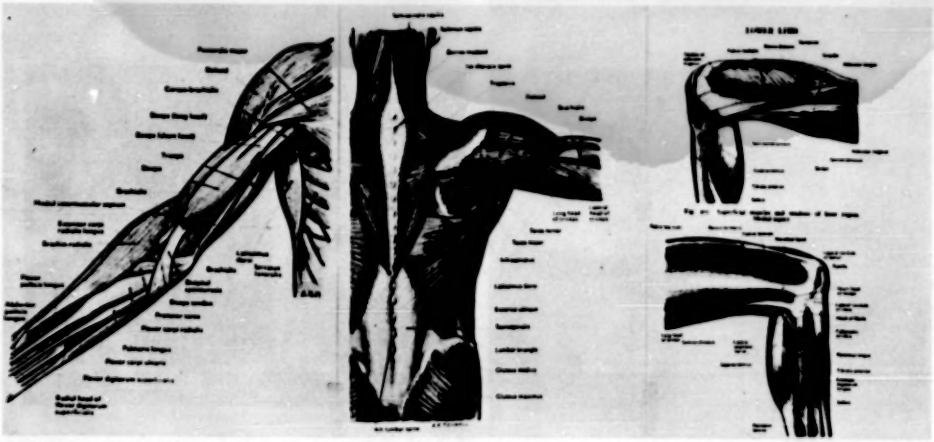
IMPROVED NUTRITION: • minimal weight loss . . . prevents muscle tissue depletion

RARE TRACHEOTOMY: • (none in this series - 664 cases)

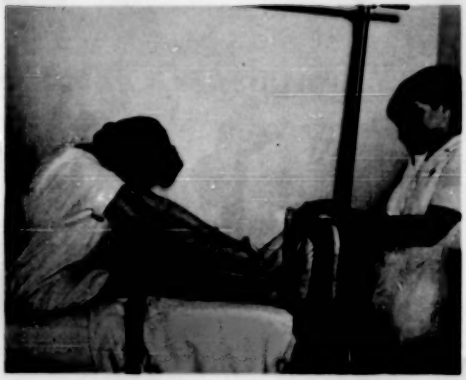
POSITIVE THERAPY MEANS
- no residual muscle or joint pain
- no contractures
- maximal joint mobility
- no ankylosis
- minimum wheelchair patients (of 664 patients - 6 wheelchair cases)

Relaxation of muscles . . . relief of pain . . . are fundamental in

POSITIVE THERAPY REGIMEN

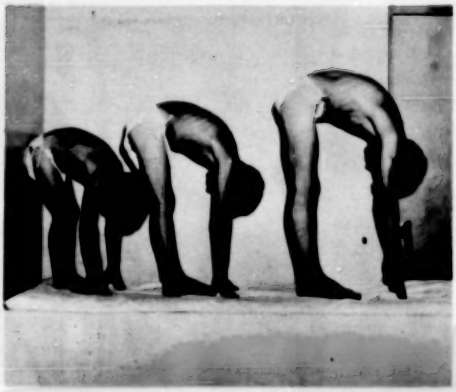


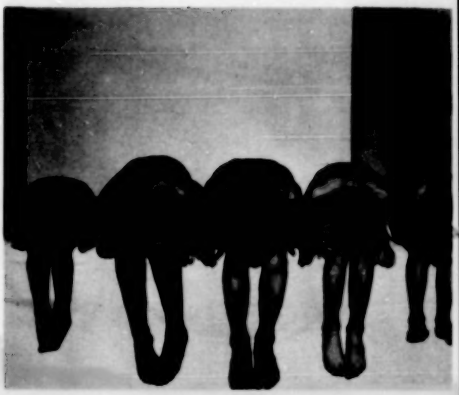
Detailed knowledge of musculature is essential in locating weakness of individual muscle groups.

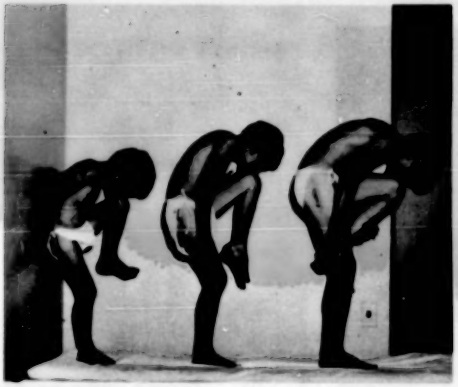


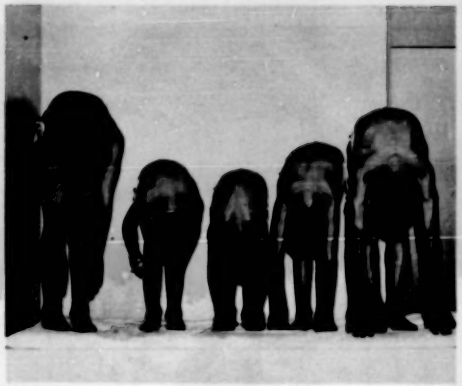
Exercises are begun while the patient is still in bed, using fracture board, footboard and trapeze.

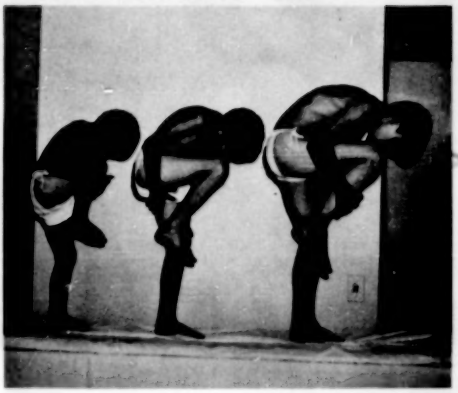
At left, a patient suffering paralysis of the hips and lower extremities uses an overhead bar to move in and out of bed. Patients are encouraged to do things for themselves.











Exercises of this type show full range of motion in all joints. Children take quickly to the "kiss the knee" exercises above and at right.